

# PROGRESSIVE MEDICINE











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1914

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PUBLISHED QUARTERLY

BY

LEA & FEBIGER

708 SANSOM STREET

PHILADELPHIA

*Awarded Grand Prize, Paris Exposition, 1900*

# PROGRESSIVE MEDICINE

A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES  
AND IMPROVEMENTS

IN THE

## MEDICAL AND SURGICAL SCIENCES

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VOLUME II. JUNE, 1914

HERNIA—SURGERY OF THE ABDOMEN, EXCLUSIVE OF HERNIA—GYNECOLOGY—  
DISEASES OF THE BLOOD. DIATHETIC AND METABOLIC DISEASES.  
DISEASES OF THE SPLEEN, THYROID GLAND, NUTRITION, AND  
THE LYMPHATIC SYSTEM—OPHTHALMOLOGY.



LEA & FEBIGER  
PHILADELPHIA AND NEW YORK  
1914

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# PROGRESSIVE MEDICINE.

JUNE, 1914.

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## HERNIA.

BY WILLIAM B. COLEY, M.D.

**Femoral Hernia.** The inguinal route for femoral hernia has again been strongly advocated by Seelig and Tuholske,<sup>1</sup> of St. Louis. They call attention to the recent contributions to the literature of femoral hernia by Moschcowitz,<sup>2</sup> Lance,<sup>3</sup> and Didier,<sup>4</sup> and state, "there are certain fairly well-rooted misconceptions regarding femoral hernia that call for correction." (1) That the repair of a femoral hernia is a simple operation. (2) That recurrence is a great rarity. (3) That the technique for femoral hernia does not require any anatomical exposure of the operative field. They state that "the fallacy regarding the simplicity of repairing a femoral hernia is easily demonstrated by witnessing a hospital house-surgeon, thoroughly competent to do routine operative work, attacking his early series of femoral herniae; if this does not furnish conclusive evidence, one has only to tackle a femoral hernia of the variety with a small empty sac surrounded by a large clump of preperitoneal fat in an obese subject, or better still, a strangulated femoral hernia requiring intestinal resection, and presenting the difficulty of pulling down sufficient healthy bowel to perform an anastomosis."

They take direct issue with the statement that femoral hernia does not recur if only the sac is ligated and no attempt is made to close the ring. This is the operation that has been strongly advocated by Ochsner, of Chicago.

My own opinion, expressed in previous articles in PROGRESSIVE MEDICINE, is thus far in accord with the authors. They believe that the same three factors which are supposed to be safeguards against recurrence in inguinal hernia, are equally essential in femoral hernia, namely: (1) High ligation of the sac; (2) snug closure of the internal ring, with

<sup>1</sup> Surgery, Gynecology, and Obstetrics, January, 1914.

<sup>2</sup> New York State Journal of Medicine, October, 1907, p. 396.

<sup>3</sup> Gaz. d. Hôp., Paris, 1912, No. 38, p. 1941.

<sup>4</sup> Cure Radicale de la Hernie Crurale, Paris Thesis, 1912.

secure buttressing of the abdominal wall; and (3) aseptic wound healing. They call attention to the large proportion of recurrences after femoral hernia operations as noted in a number of large statistics, *e. g.*, Bresset observed 395 cases of femoral hernia, 232 of which were operated upon without closure of the femoral ring, with 29 per cent. recurrences; 163 which were operated upon with closure of the ring, showed 8.6 per cent. of relapses. Moschcowitz<sup>1</sup> reports an interesting case in which he had operated for femoral hernia and had secured an apparently ideal result. About one and a half years later he was obliged to perform a laparotomy on the same patient. Examination from within the abdomen revealed a recurrence, the sac being two inches deep. Pott<sup>2</sup> analyzed 422 cases of femoral hernia and found that there was 36.7 per cent. of recurrences in the cases in which the femoral ring was not sutured, and 28.4 per cent. of recurrences in the cases in which the ring was sutured. (The methods used for closing the ring were such that secure closure was impossible.)

The writers lay great stress upon the third point, namely, that an anatomical exposure of the field is not essential in the operation for the cure of femoral hernia, saying that "possibly the reason why anatomic exposure has not been considered necessary is that the vast majority of femoral herniae are repaired by the crural route; and when a femoral hernia is attacked through a thigh incision, it is physically impossible to secure an anatomic exposure. This statement is beyond all doubt or question, and may be proved easily by anyone who will take the time to dissect the region of the femoral ring and canal." Their paper is accompanied by very excellent anatomic drawings which I take pleasure in reproducing. They state it is unfortunate that probably the most important structure utilized in the closure of the femoral ring, *i. e.*, Cooper's ligament, is neither adequately described nor pictured in any of the anatomies. They further declare that a properly performed operation for the cure of femoral hernia by the inguinal route renders it possible to outline the structures in and about the femoral ring as clearly as they are pictured in the illustrations, except in very stout subjects. A brief description only of the operation can be given here. (For full details see article itself.) Its steps consist in:

1. A three to four inch incision in the inguinal region, continued downward under the thigh.
2. Division of the aponeurosis of the external oblique in the direction of its fibers.
3. Dissection of the aponeurosis of the external oblique, as in the ordinary Bassini operation, with freeing of the cord, which is held to one side with a tape; exposure of the transversalis fascia, which is nicked and divided.

<sup>1</sup> Loc. cit.

<sup>2</sup> Deutsch. Zeitschr. f. Chir., 1903, vol. lxx, p. 556.

4. Opening of the peritoneum as it converges to form the neck of the sac, through which the contents of the sac are pulled and placed in the peritoneal cavity. If the intestine is strangulated, it may be freed by cutting Gimbernat's ligament.

5. Introduction of dressing forceps into the sac to its lowest point, then closing forceps upon the sac, evertting it by withdrawal of the forceps; the sac is then tied off by transfixion ligature or suture.

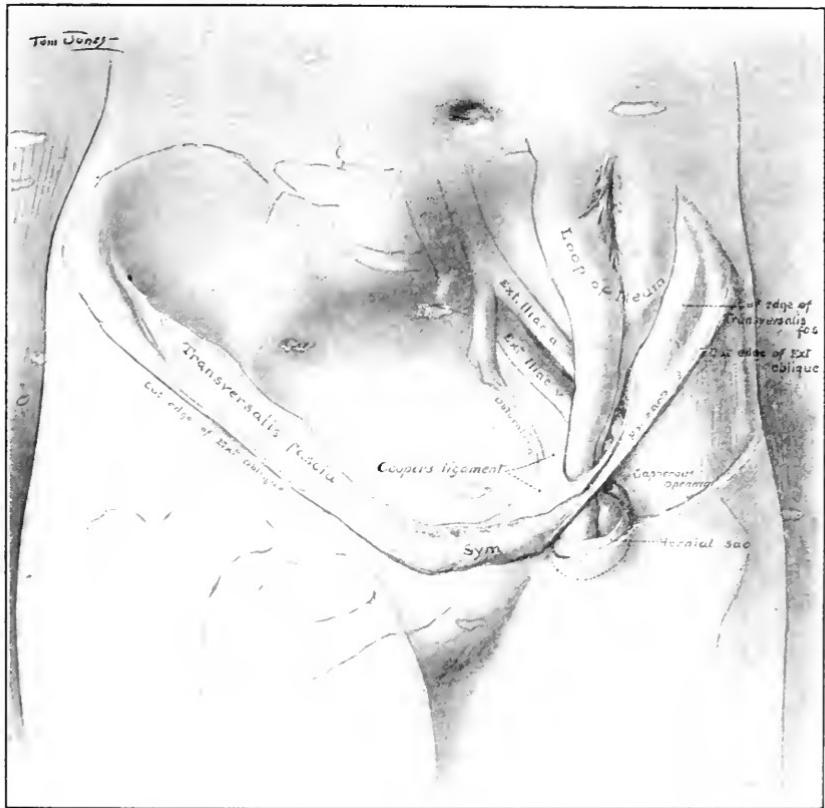


FIG. 1.—Dissection of female pelvis to show the structures forming the femoral ring. The pelvis is tilted slightly forward and is viewed slightly from the right side.

6. Closure of the femoral ring which is accomplished in the following manner: The ring is exposed to full view by retracting the lower flap of the external oblique downward and outward and by retracting the skin, the upper flap of the external oblique, the tendon of internal oblique and transversalis muscles and the transversalis fascia upward and inward (Fig. 3). It is pointed out that when the parts are retracted as described, one can palpate the horizontal ramus of the pubis and can see it covered by a dense, tough, white, glistening, white fascial membrane. This membrane is Cooper's ligament. With a small, full curved

needle, one takes a deep bite through Cooper's ligament just internal to the iliac vein and then another bite through the lower flap of the transversalis fascia and the edges of Poupart's ligament. Another suture is similarly placed internal to the first one, and a third one still further internally, if necessary. The most internal suture always picks up Gimbernat's ligament. When these sutures are tied, they approximate Poupart's to Cooper's ligament and effectually close the hernial orifice.

7. Closure of the wound as in ordinary inguinal hernia.

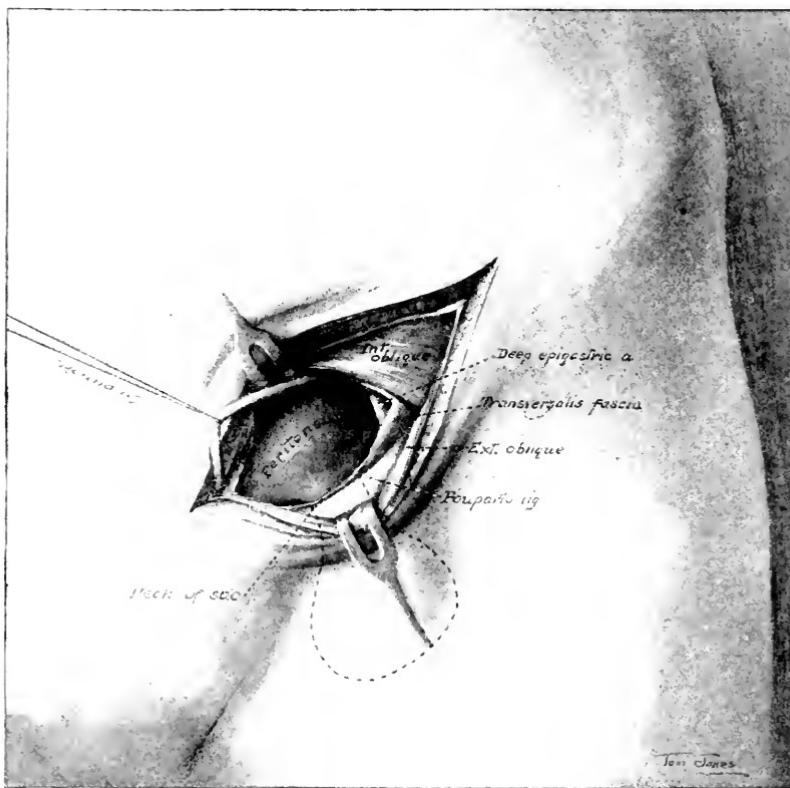


FIG. 2.—Skin, subcutaneous tissue, external oblique and transversalis fascia have been incised and the upper and lower flaps retracted upward and downward respectively.

They state that the operation is practically identical with the description furnished by Moscheowitz.

In a supplementary note, the authors emphasize the great importance of Cooper's ligament. They believe that the same has been very inadequately described in most of the text-books on anatomy, and call attention to the fact that although Sir Astley Cooper described

the ligament which bears his name, one cannot find the ligament in his own book unless one has discovered in advance what the ligament is. Cooper describes the os pubis as being "covered by a ligamentous expansion, which forms a remarkably strong production above the linea iliopectinea, extending from the tuberosity of the pubis outward and projecting from the bone over that line." Later he refers to this ligament as "the ligament of the pubes," thus establishing the identity

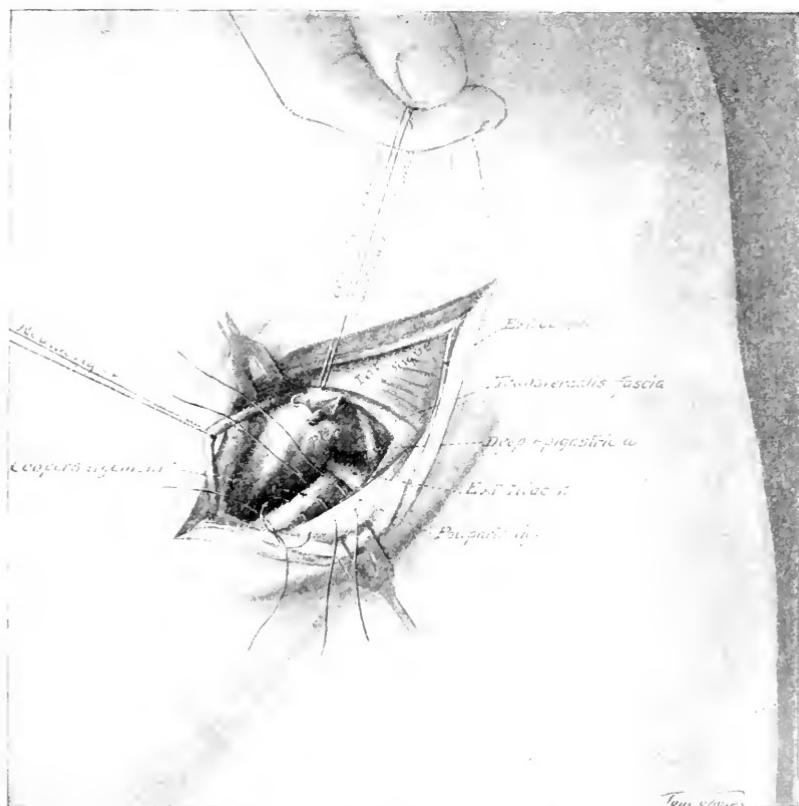


FIG. 3.—The sac has been delivered, ligated high, and amputated. The three chromic gut sutures for closing the femoral ring are in place, ready to tie.

of this structure with the "ligamentum pubicum." Of course, Cooper never utilized this ligament for closing a hernial ring, for in the days of Cooper, hernial rings were not closed. They add that Cooper's own description being inadequate, it is necessary to supplement it by investigations of modern anatomists. The three best descriptions, in the opinion of the authors are those of Poirier and Charpy, Testut and Eisler (in Bardeleben's Handbuch).

As I have already stated in previous criticisms of the inguinal route

for femoral hernia, while it is a very beautiful operation anatomically, and doubtless would give admirable results in the hands of skilful operators, such a complicated operation ought never to be recommended for general use, until it has first been proved that it is impossible or difficult to obtain equally good results by simpler methods. This is the attitude that I have taken for many years, and increasing experience with the simpler methods only confirms my conviction. While fully agreeing that the operation for femoral hernia is not one for the house surgeon to perform without proper instruction by a more experienced surgeon, I still maintain that an operation but little more difficult or prolonged than the simple removal of the sac without closure of the ring, as advocated by Ochsner, will give almost ideal results, if properly performed. The main steps of this operation I have frequently described. They are:

An oblique incision is made one-quarter to one-half inch below Poupart's ligament and parallel with it, almost identical with the incision made for inguinal hernia, only slightly lower and a little shorter. The sac, with the mass of extraperitoneal fat that almost always surrounds it, is then freed well up into the femoral opening. The masses of fat are carefully removed, the sac itself, by gentle traction, is brought down well beyond its neck to a point where it widens into the general peritoneal cavity. It is always opened before ligature, so as to make sure that it is empty. If omentum is present, this is tied off and removed. The ligature having been placed well beyond the neck by transfixion, it is carefully tied and the sac removed. When the stump of the sac has been pushed through the opening into the abdominal cavity, there is no longer any funicular process present in the femoral region. With a curved Hagerdorn needle, threaded with kangaroo tendon of medium size, the suture is placed as follows: The needle is first passed through the inner portion of Poupart's ligament or the roof of the canal, then downward, taking firm hold of the pectineal fascia and muscle, then outward through the fascia lata overlying the femoral vein, and finally upward, emerging through the roof of the canal about one-quarter inch distant from the point of entrance. Upon tying this suture, the floor of the canal is brought into apposition with the roof, and the femoral opening is completely obliterated. The skin and superficial fascia are closed by means of an interrupted catgut suture and a sterile dressing is applied, without drainage. The first change of dressing is made at the end of one week. The patient is kept in bed for two weeks and allowed to go home at the end of two and a half weeks. A firm spica bandage is worn one week after leaving the hospital, at the end of which time no further support is needed.

The main and important factors of success are the complete removal of all the extraperitoneal fat, freeing the sac from the femoral canal and bringing it down at least a half to one inch below the normal level

of the neck, removal so high up that, when the stump has been replaced within the canal, there is no longer any pouch or dimpling process of the peritoneum; closure of the femoral canal by purse-string suture of kangaroo tendon.

That this comparatively simple operation is sufficient in the great majority of cases of femoral hernia, is evident from the statistics of the Hospital for Ruptured and Crippled, supplemented by my personal results. I have operated upon upward of 200 cases with only one relapse. These cases include all types and sizes of femoral hernia, and the results, I believe, justify the position which I have long held, that there is no reason for adopting the far more complicated, though theoretically more ideal, operation described by the authors. At any rate, the operation should not be adopted until the men who so strongly advocate it show by a large series of cases, traced for a long period of time, that the final results are superior to those obtained by the other, simpler methods.

**Inguinal Hernia. THE TREATMENT OF INGUINAL HERNIA IN CHILDREN.** Hertzler,<sup>1</sup> of Kansas City, discusses the treatment of inguinal hernia in children. He states that the diagnosis of hernia in children offers no difficulty.

While this is true, as a rule, there are certain exceptions which it is well to know. I have been called upon by a prominent specialist in children's diseases to operate on an infant for a supposed strangulated hernia, when the actual condition was a small hydrocele of the cord. The diagnosis between these two conditions seems extremely difficult, and can be made only by a careful study of the general condition of the child. The tense tumor at the external ring or possibly occupying the canal may simulate exactly the tumor formed by a strangulated hernia. It is only the absence of general constitutional symptoms, the fact that there has been no interference with the passage of the bowels, that enables one to make an accurate diagnosis in these cases.

Hertzler has little faith in the possibility of a cure by mechanical treatment of hernia in children. He states that palliation is still largely practiced chiefly by two classes of persons: those who are opposed to operation by principle, and those who employ palliation from necessity. Those who oppose radical cure from principle, he divides into two classes: those who still believe that hernia may be cured by the truss and those who have met disaster in radical treatment. Among the latter may be mentioned Gruenert<sup>2</sup> who had three deaths in thirteen patients, which caused him to advise against operation during the first three years. Hertzler's conclusions are:

1. All inguinal hernias in children are due to the persistence of the processus vaginalis.

<sup>1</sup> Journal of the American Medical Association, November 22, 1913, p. 1879.

<sup>2</sup> Deutsch Zeitschr. f. Chir., 1903, vol. lxviii, p. 518.

2. Inguinal hernias are not cured by the truss and rarely recover spontaneously.

3. Surgery is permissible in all cases if the facilities are of the best and the operator is skilful. Operation is urgent if the hernia protrudes persistently or if the child is annoyed greatly by retentive appliances which lessen his activities or produce excoriations. Operation is demanded if the hernia is irreducible or strangulated.

4. Because of the difficulty of maintaining an aseptic field after operation, it is wise conservatism to wait until the child has reached such an age as will enable him to lend his coöperation, *i. e.*, until about the fourth year.

5. Palliation is demanded when organic disease is present or adequate facilities for operation are not at hand.

With most of these conclusions I agree, particularly as regards the wisdom if waiting in the ordinary case until the child has reached the age of three or four years. With the second conclusion, that inguinal hernias are not cured by a truss and rarely recover spontaneously, I cannot agree. At the Hospital for Ruptured and Crippled, where we have an average of nearly 1000 cases of hernia in infants and children yearly, on one occasion I made a study of the after-history of these infants and children. This study proved beyond question that a considerable number are permanently cured by mechanical treatment, or that a cure resulted spontaneously. After the child has reached the age of three or four years, I believe this number is very much smaller than in infants. My reason for not advocating operation in infants is not the one which influenced Gruenert, as I have met with no disaster in the radical treatment at this early age; in fact, we have had a group of over 20 cases of strangulated hernia operated upon at the Hospital for Ruptured and Crippled under the age of two years, without a single death. The chief ground for the conservative position which we have all held at the Hospital for Ruptured and Crippled for many years is the fact that a very considerable number of cases below the age of four years is actually cured by truss. Therefore, it is unwise to subject all of them to operative treatment, even though the surgical risk is extremely small. If a hernia cannot be well held with a truss and it is difficult or impossible to carry out proper mechanical treatment in any individual case, I would not hesitate to advise radical operation, no matter what the age of the infant.

**Umbilical Hernia.** The use of the *subcutaneous elastic ligature* in the treatment of umbilical hernia in children, has been recently advocated by Fraser,<sup>1</sup> of the Royal Hospital for Sick Children.

While acknowledging the strong tendency toward spontaneous cure of this variety of hernia in children, which may be hastened by simple mechanical aids, he calls attention to two disadvantages of

<sup>1</sup> London Lancet, September 27, 1913, p. 925.

mechanical treatment by means of pads or inversion of the abdominal wall. (1) The degree of uncertainty which surrounds the prospect of an early cure; (2) the duration of time during which retention treatment is required, at least six months being necessary, more often a year or even two years. To parents and patients alike, such prolonged treatment, he believes, becomes intolerably irksome. About a year ago, he was glad to adopt the new treatment by an elastic ligature brought out in a paper of Brun's.<sup>1</sup> It is Brun's method, somewhat modified, that he has employed.

As regards the indications for the operation, Fraser states that it should not be performed in children under six months of age. In the majority of cases, it is better to wait until the child is one year old. Upon the size of the opening in the abdominal wall depends the suitability of the subcutaneous elastic ligature. A large opening is unsuitable for operation by this method, as there is later a tendency to recurrence. The rough guide which one uses is the tip of the little finger—an opening which is large enough to admit this is considered unsuitable. It is essential that the sac be empty; irreducible contents of any description must be regarded as an absolute contra-indication.

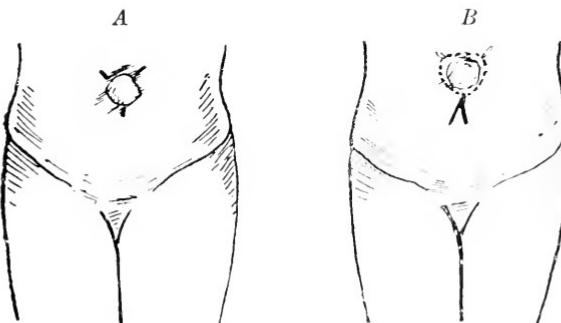


FIG. 4.—*A*, showing radiating skin incision around the herniae. *B*, second stage of the operation. The elastic ligature is lying in position. In practice it lies more closely around the pedicle of the sac.

The *technique of the operation* is briefly as follows: The skin over the fundus of the protrusion is grasped with a pair of dissecting forceps, and skin and sac are pulled gently upward from the abdominal wall. Great care is exercised to ascertain that the contents of the sac are completely reduced. Three small incisions are made at equal intervals around the periphery of the sac, at the point where the skin is reflected on to the abdominal wall (Fig. 4). These incisions penetrate the skin and subcutaneous tissues, but they must not injure the sac. With a blunt dissector it is now possible to undermine the tissues around the pedicle of the sac. The elastic ligature is now pulled beneath the skin,

<sup>1</sup> Arch. de Méd. des Enf., Paris, September, 1912.

following the track of separation (Fig. 2). When the ligature is in position, the operator, having satisfied himself that the sac is empty, pulls the ligature as tightly as possible around the pedicle of the sac and fastens it so with a stout piece of silk. The ends of the elastic ligature are left protruding through one of the incisions and are cut to a convenient length; a simple dressing is applied and kept in place by means of a band of adhesive plaster.

The ligature is allowed to remain in place for six days, when it is removed by cutting the silk knot. The opening which it leaves quickly closes. A dressing is worn until the wounds are healed.

Fraser states that the method has been used in 21 patients, and that the results have been uniformly satisfactory. The first case proved the permanency of the cure: About two days after operation the child developed whooping cough, but, in spite of the persistent coughing and straining, there was no recurrence.

He summarizes the *advantages of the operation* as follows: The operation is essentially of the most simple type. The after-treatment is brief and satisfactory. The cure is apparently a permanent one.

Personally, I am strongly opposed to the adoption of any such method of treatment in umbilical hernia in children. If the operation is limited to herniae with an opening no larger than to admit the tip of the little finger, it is applicable only in a group of cases that would be almost certainly cured by simple mechanical methods, the best of which is the application of a small pad, preferably a wooden button mold covered with rubber plaster, held in place by a two-inch strip of plaster surrounding the body of the child. After an experience of over twenty-three years with this method at the Hospital for Ruptured and Crippled, I am convinced that the results are ideal and that, in the great majority of cases, the treatment does not need to be sufficiently prolonged to be "intolerably irksome." As a matter of fact, in most of the cases with an opening of this size, a cure ensues spontaneously, and, in view of this, we do not think it justifiable to adopt a radical operation, even though it be one of no greater magnitude than the elastic ligature. Infection might easily occur in such an operation, in fact, it would be much more likely to occur than in the ordinary operation of removal of the umbilicus. If any operation at all is to be performed, I believe the open operation of removal of the umbilicus and careful suturing, to be much preferable, occupying little more time than the elastic ligature, and being much more likely to yield a lasting result. It is seldom necessary to operate upon umbilical hernia in children under the age of fourteen years.

**Inguinal Herniotomy.** Judd,<sup>1</sup> of Rochester, recommends a single *transverse incision in double inguinal herniotomy*. He makes a transverse incision from 8 to 12 cm. long, or longer in fleshy patients, from

<sup>1</sup> Old Dominion Journal of Med. and Surg., Richmond, Va., April, xvi, No. 4, pp. 153 to 211.

a point midway between the internal and external abdominal rings on one side to a similar point on the opposite side, thus connecting the two inguinal canals.

While this incision may have something to recommend it in very stout persons, I think there are few exceptions when the two ordinary oblique incisions over the inguinal canal would not be preferable. It may be added that the combined length of the two incisions would not more than equal the length of the transverse incision and gives better access to the canal.

**The Use of Three Flaps of Periosteum for the Closure, or Securing of Large Hernial Apertures,** is advocated by Henschen.<sup>1</sup> He has reference principally to the spontaneous and postoperative herniae of the median line, where successful and permanent closure of the aperture is rendered difficult by the scarcity and weakness of the anatomical material.

He briefly reviews the methods of Witzel, Goepel, Barlett, MacGavin, *et al.*, who achieved good results with the implantation of silver wire and filigree nets. On the other hand, he refers to Riem's<sup>2</sup> exhaustive paper on the ultimate fate of the silver wire nets inserted in the hernial openings. Riem's report covers 20 cases operated upon at Körte's clinic, with the following result:

In four, the implanted net had to be removed, owing to persistent secretion. Of the remaining sixteen, eleven were traced up to eight years since the time of operation. His conclusions are: "The hope that a wire net would permanently retain its form and firmness, and mechanically close a defective spot in the abdominal wall, has not been realized." He found that the silver wire gradually becomes affected by the secretions of the body; that it becomes eroded and finally breaks. While the fragments have usually been found embedded in dense and strong cicatricial tissue, the possibility of wire ends becoming exposed, he states, is by no means excluded. Furthermore, the *x*-rays show that the net sometimes changes its location, thus subjecting the large vessels to the danger of puncture by protruding ends of wire. Only one of eight filigree nets that had been radiographed had fully retained its original shape and structure. All the others were completely broken up. All this, Henschen states, goes to show that these wire nets by no means afford an ideal material for closing abdominal apertures. The same would seem true of all heterogeneous substances.

His own case was a hernia the size of two fists which developed above the symphysis after operation. None of the myoplastic methods seemed to promise success, hence, he decided to close the large opening by stitching a periosteal flap upon the same. A strip of periosteum 16 cm. long was derived from the inner surface of the tibia. This was cut in two, and stitched transversely upon the aponeurosis covering an area

<sup>1</sup> *Beit. z. klin. Chir.*, Band lxxvii, Heft 1, 1912.

<sup>2</sup> *Arch. f. klin. Chir.*, Band xciii, p. 917.

of 8 x 8 cm. Primary union followed. Examination about six months after operation showed a strong, hard, plate at the site of the plasty, and, while there was no sign of a recurrence at the former hernial site, two beginning (bilateral) small, inguinal herniæ were noticed. Henschen states that König has used such periosteal flaps for the closure of all large hernial openings, fourteen times, and he believes with König that the method deserves to be further developed.

In the same number of the *Beiträge z. klinische Chirurgie* (Band lxxvii, Heft 1, 1012), Hans Brun contributes an article on the

**"Technique of the Operative Cure of Large Abdominal Herniæ,"** etc. He states, the etiology of herniæ, their localization, and anatomy, as also their size and the length and form of the suture resulting after operation, are so variable, that no one method of securing the suture could be applied to all cases, and, while the transverse suture represents a great advance in the therapy of umbilical hernia, and the plastic utilization of the recti and their sheaths may often be of value in cases of median abdominal hernia, there are, nevertheless, cases where the hernial opening is of such size, and the local material so brittle that heterogeneous implantations have to be resorted to. In these extreme cases, he states, the use of silver wire nets has proved of great value. He reports two personal cases:

CASE I.—Woman, aged fifty-two years; hernia the size of a seven months' gravid uterus; implantation of a net 8 x 10 cm. in size, with rounded-off corners. The patient made a good recovery, and was out of bed on the twentieth day after operation. This patient was frequently reexamined and, while the shape of the net seemed to have changed soon after operation, the hernia never relapsed nor did the patient ever complain of annoyance from the presence of the net. She died five years after operation, of a malignant ovarian tumor.

CASE II.—Laundress, aged thirty-two years; had a large ventral hernia following a number of abdominal operations. Four unsuccessful attempts had been made to effect a cure of the hernia. When admitted to Brun's clinic, the patient showed an abdominal hernia the size of a man's head. Operation May 25, 1906, silver filigree 8 x 10 cm. was used; primary union. Patient was out of bed on the fourteenth day after operation. For over a year she remained well, then she began to complain of stitch-like pains in the abdomen which persisted, although they had become less severe than at first. The accompanying radiograph (Fig. 5) shows the condition of the net five and a half years after the implantation.

In view of this experience, Brun states that were he again to operate on such a large abdominal hernia requiring the implantation of the silver net, he would modify the latter and have it made of interlinking small silver rings, as shown by Fig. 6. The superiority of this kind of net is evident.

The method of the IMPLANTATION OF SILVER WIRE or filigree for the cure of large herniae has been very fully discussed in previous volumes of PROGRESSIVE MEDICINE. After reviewing a large series of cases

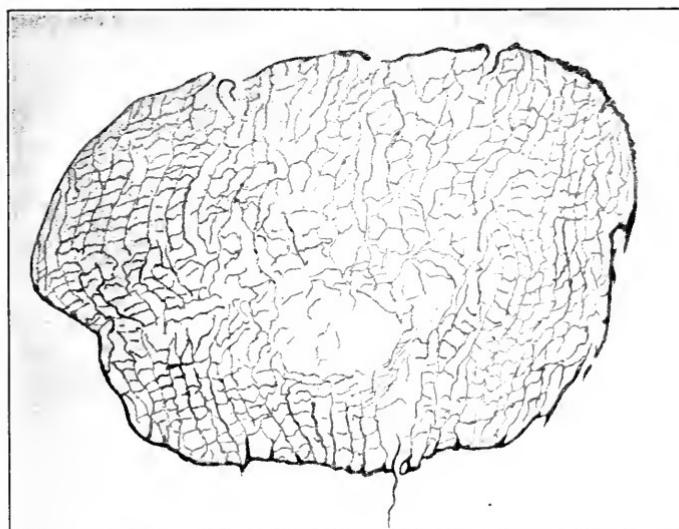


FIG. 5

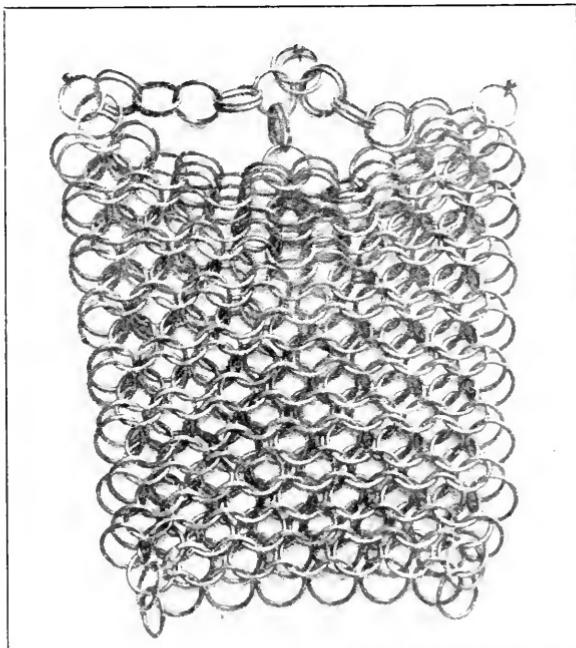


FIG. 6

reported by McGavin,<sup>1</sup> 146 in number, I said: "What happens to these filigrees of silver wire after they have remained a long time within the tissues, is a question which, up to the present time, has not been answered fully. That they occasionally cause sinuses long periods after operation, I have repeatedly observed in cases that have come to the Hospital for Ruptured and Crippled. Personally, I believe that there are very few of these so-called cases 'incurable by other methods,' that cannot be quite as satisfactorily repaired by some method of overlapping the normal structures, either muscle or fascia."

I think attention should be called to the fact which was brought out in the discussion of McGavin's paper in the Royal Society of Medicine. Hutchinson said that McGavin had found it necessary to use the filigree in a very large proportion of all cases of hernia upon which he had operated, *e. g.*, in a total of 314 cases operated upon, the filigree was used in 166; or of 263 cases of inguinal hernia, filigree implantation was done in 106, or about 40 per cent. Hutchinson stated that on looking up the records of recent operations at the London Hospital, he found that the filigree had been used in only 1 out of each 100 cases. He believed McGavin's statement "that the use of filigree was the only radical cure for hernia," to be an exaggeration. If it had been said that filigree implantation was an admirable method in very large hernias, this statement would have found general agreement.

It should be noted that the American surgeons, who have advocated the method of filigree implantation, notably Bartlett, Meyer, and Wiener, would use it only in cases of very large ventral or umbilical herniae. As I have already stated on a number of occasions, I believe there are very few cases of inguinal hernia in which it is advisable to operate at all, which cannot be cured by the Bassini operation with or without the modification of the transplantation of the rectus muscle. Even in umbilical herniae I believe there are few cases which cannot be cured by the Mayo overlapping method, that would offer any prospect of a cure from filigree implantation.

**The Importance of Rectus Transplantation for Certain Cases of Inguinal Hernia** has been further emphasized by Dr. Schley,<sup>2</sup> of New York. He refers to the literature on the subject of rectus transplantation and mentions the procedure known as Bloodgood's, published in 1898 (Fig. 7), which he says is not altogether of this late date. Bassini, in 1890, recommended suture of the lower border of the rectus to Poupart's ligament in 2 or 3 sutures taken nearest the pubes. Wölfler, in 1892 (Billroth's Festschrift), reported 51 of 58 cases done by a complicated technique of his own in which the cord was transplanted back of the rectus, the internal oblique sutured to Poupart's ligament, and, lastly, the rectus drawn out of its sheath anteriorly and sutured to Poupart's

<sup>1</sup> Lancet, December 21, 1912.

<sup>2</sup> Annals of Surgery, October, 1913, p. 473.

ligament as well. Schley states "this anterior opening of the rectus sheath weakens the internal attachment of the already sutured internal oblique if it be well developed," he considers the transplantation in Wölfler's cases as a routine method, unwarranted. The recurrences were about 5 per cent. Bloodgood more recently opens the rectus sheath from behind.

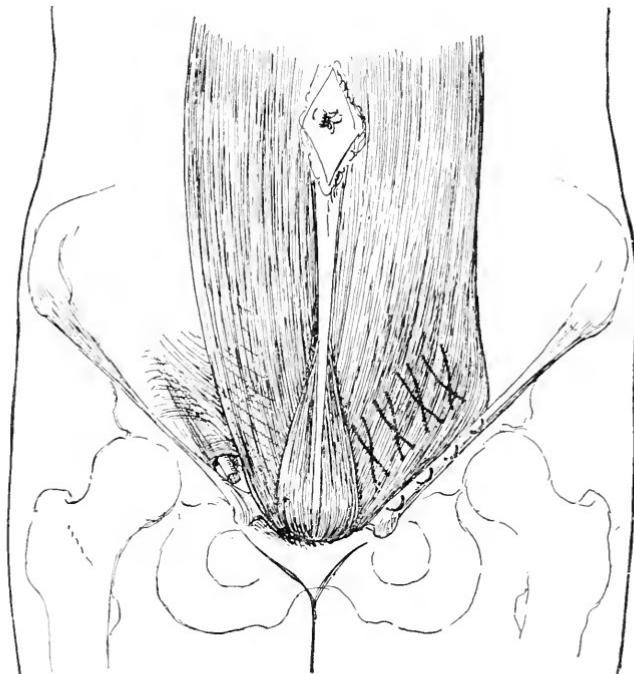


FIG. 7.—Deviation of fibers of rectus. (After Bloodgood.)

Slajmer, in 1898, reported 150 cases operated upon by a modified Wölfler method without cord transplantation. After freeing the layers, his outer two sutures bring the internal oblique to Poupart's ligament, the next two the outer part of the anterior sheath of the rectus and the rectus muscle edge to Poupart's ligament and the external oblique fascia, and the last two, the inner edge of the rectus sheath and external oblique fascia. Two final sutures close the external ring. The recurrences were about 4 per cent.

The method which Schley has followed in some 12 cases of indirect hernia, with markedly deficient internal oblique and weak transversalis fascia, has been: "to first utilize what remains of the oblique muscle, usually only that part external to the internal ring and transplanted cord, by inserting Coley's stitch. The rectus sheath was opened for three inches at one-quarter inch from its edge, the incision being below the insertion of the aponeurosis of the remaining good oblique, the muscle

loosened from its sheath and drawn down to the thoroughly cleaned shelving edge of Poupart's ligament by four No. 2 or 3, fourteen-day chromic sutures. The cord lies upon this bed. The outer half of the external oblique aponeurosis is sutured to the internal half of the rectus sheath. This overlaps the line of union of muscle to Poupart's ligament and closes over the rectus muscle. The inner half of the external oblique aponeurosis is drawn down over the line of union of the outer half with the rectus sheath with a few mattress sutures. Externally, one or two sutures of chromic gut bring into close apposition the cut edges of the aponeurosis."

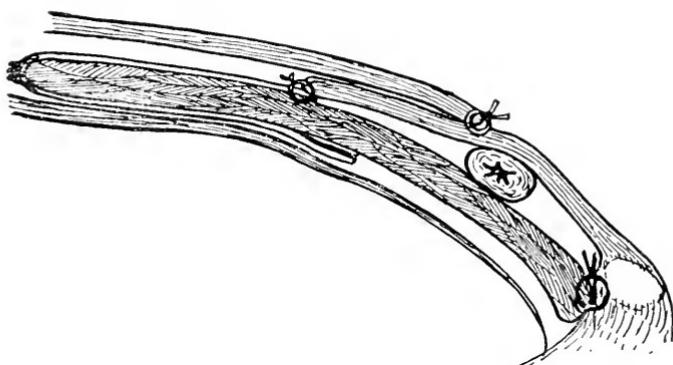


FIG. 8.—Schematic diagram of arrangement of rectus and external oblique fascia.

Personally, I believe the transplantation of the rectus muscle is almost essential to a permanent cure in most cases of large indirect hernia, and I always make use of it in inguinal direct hernia. I believe the method followed by Dr. Downes<sup>1</sup> to be the best thus far proposed. Unlike Slajmer, I regard the transplantation of the cord much more important in direct hernia than in oblique, although I believe the cord should be transplanted as a routine measure in all cases of inguinal hernia.

**Direct Hernia.** An improved method of operating on direct hernia has recently been brought out by Dr. Wm. A. Downes,<sup>2</sup> my associate at the Hospital for Ruptured and Crippled and the General Memorial Hospital. The essential features of the operation, as he performed it in 50 cases, are best stated in his own words: "A complete removal of the sac should be done as conditions will allow; in many cases the sac is divided into two portions by the deep epigastric vessels, one part above and external, an indirect hernia, and another below and internal, the direct portion. In these cases the vessels should always be divided, thus forming one sac. As a matter of fact, all indirect herniae should be explored by passing the finger through the neck and testing the

<sup>1</sup> Loc. cit.

<sup>2</sup> Annals of Surgery, 1911, vol. liii, p. 568.

condition of the posterior wall of the inguinal canal. Frequently, a weakness will be found which was not suspected. A frank sac might not always be present, but it is in just such cases where there is a weakness that recurrence takes place, and in which the additional safeguard of rectus transplantation is indicated.

After the sac has been disposed of, the internal oblique and transversalis are held up by a small, blunt retractor placed at the internal ring, and these muscles are followed, down and in, until they join the transversalis fascia at the outer margin of the rectus. The sheath of the rectus, formed by these structures at this point, is opened, and the muscle is exposed down to its pubic attachment. Three sutures of kangaroo tendon are now taken between the outer margin of the muscle and Poupart's ligament, which has been completely freed and exposed by proper retraction. The sutures should be placed from below upward, and about one-half to three-quarters of an inch apart. A fourth suture might be necessary. After all sutures are placed, gentle traction should be made, drawing muscle and ligament well together, and while thus held by an assistant, the sutures should be tied in the order of their insertion."

In his earlier cases, Dr. Downes split the aponeurosis of the rectus on its upper surface, turned it down with the muscular fibers, and sutured it to Poupart's ligament, but in a number of instances the lower part of the muscle was found to be so thin that this incision went through, and when the sutures were tied, a weak area, triangular in shape, was left in the muscle.

"The retractor is now removed from beneath the internal oblique and transversalis muscles, and the usual Bassini operation performed from above downward, the sutures catching Poupart's ligament just superficial to and between those of the first row. The external oblique is then closed in the usual way. It is thus seen that there are three distinct layers, and not only the weak but the often absent posterior wall of the inguinal canal has been strengthened as it could be done in no other way. The cord is always transplanted. If the cremaster muscle is thin and frayed, it had best be cut away; if, however, it is thick and strong, it should be included in the sutures uniting the rectus with Poupart's ligament."

Dr. Downes states that all of his cases have healed by primary union, and thus far the results have been uniformly good. Ten have been traced for more than one year. One case was operated upon in November, 1909, for double direct hernia. The patient's occupation is that of a prize fighter, and he stated that he had felt like a new man since the operation. In this case, the epigastric vessels were divided on both sides.

The annual report<sup>1</sup> of the Hernia Department of the Heidelberg

<sup>1</sup> *Beit. z. klin. Chir.*, 1913, Band lxxxvi.

Clinic for the year 1912, shows a total of 475 admissions—395 men, 81 women—with 9 deaths. Local anesthesia was used in the majority of operations upon adults. 361 of these cases were inguinal hernia, 329 men, 32 women—with 3 deaths. Bassini's operation was generally used in adults, and Ferrari's in children. 62 were double hernia; 7 of the cases were not operated upon, and, in 10, the operation was done for recurrence.

Forty-one cases of crural hernia are recorded, 16 in men and 25 in women. The usual radical operation with suture of Poupart's ligament to the periosteum of the pubic bone, or pectineal fascia, was employed. There were 12 operations for umbilical hernia (11 males and 1 female), one of which was an operation for a recurrence. After ligation of the sac, the hernial opening was closed by layer sutures. 23 of the cases were postoperative ventral herniae (13 males, 10 females). 19 were epigastric herniae (17 males and 2 females).

Of 44 cases of incarcerated hernia (24 males, 20 females), 22 were inguinal, 17 crural, and 5 umbilical hernia, with 6 deaths.

The youngest patient with incarcerated inguinal hernia was fourteen weeks old. One was a recurrence after a former operation for hernia.

**Results of Operation for Radical Cure of Hernia at the Hospital for Ruptured and Crippled, New York.** At the Hospital for Ruptured and Crippled, from December, 1891, to January, 1914, we have performed 4285 operations, of which 3136 were for inguinal hernia in the male; 3119 indirect, with 21 recurrences = 0.67 per cent., and 17 direct, with no recurrences. 776 operations were performed for inguinal hernia in the female, namely, 510 in children, with 1 = 0.19 per cent. recurrence, and 259 in adults, with 12 recurrences = 4.63 per cent.; 7 direct with 1 = 14.2 per cent. recurrence; 181 femoral herniae, 59 of which were in children, with no recurrence, and 122 in adults, with 6 = 4.92 per cent. recurrences. Umbilical, 111, of which 34 were in children, with no recurrence, and 77 in adults, with 3 = 3.8 per cent. recurrences. Ventral, 68; that is, 16 in children, without recurrence, and 52 in adults, with 10 = 19.2 per cent. recurrences. Epigastric, 12, with 1 recurrence, = 8.3 per cent., and lumbar 1, without recurrence.

As regards the method of operation, the typical Bassini operation was performed in the great majority of the cases of indirect inguinal hernia in the male, *e.g.*, in 2441 cases, with 12 recurrences = 0.49 per cent.; in 678 the cord was not transplanted, showing 10 relapses = 1.4 per cent. As regards the direct type, Bassini's operation, with transplantation of rectus, was done in 17 cases, with no recurrences. For umbilical hernia we are now using the Mayo, or overlapping, method with great improvement over former results, *i.e.*, in 80 cases operated upon by the Mayo method there was 1 = 1.2 per cent. recurrence; in 31 cases operated upon without overlapping, there was 2 = 6.4 per cent. recurrences. In 32 cases which were strangulated, there was one

recurrence, or 3.1 per cent.; 61 operations were due for superficial inguinal and interstitial hernia, without recurrence, and 231 operations for undescended testicle associated with hernia, with no recurrence. The total number of deaths was 8 = 0.18 per cent.

The results of operation at the Hospital for Ruptured and Crippled from 1891 to 1914 show that in 181 cases of femoral hernia there were 6 relapses, 4 of which occurred after operation for a previous recurrence.

Separating the children from the adults, we have 59 cases in children without relapse, and 122 in adults, with 6 relapses or 4.92 per cent.

Personally, I have operated upon over 100 adult patients outside of the hospital, with only one relapse.



FIG. 9.—Showing the inguinal canals exposed by splitting the fibers of the external oblique fascia and retracting the flaps. The right side presents the condition normally found, namely, a well-defined conjoined tendon attached to the crest of the pubes. On the left, the muscle fibers of the internal oblique and transversalis are seen to pass directly inward to be inserted high up on the rectus, and no conjoined tendon is formed. This disposition of the muscles creates a triangular space whose base is the rectus, and whose sides are formed by the internal oblique and transversalis and Poupart's ligament; the floor of this space is formed by the transversalis fascia.

Hessert,<sup>1</sup> of Chicago, gives an admirable and concise description of the conjoined tendon, elucidated by a very good illustration. Hessert states:

"The conjoined tendon is formed by the aponeurosis of the transversalis, together with the more medial lower portion of the internal oblique, these two layers of fascia uniting in this region to form this so-called conjoined tendon, which is inserted into the body and superior ramus

<sup>1</sup> Surgery, Gynecology, and Obstetrics, May, 1913, p. 566.

of the pubis. Medially, it is especially thickened to form a band, the falk inguinalis, which is firmly attached to the tendon of the rectus.

"Deviation from the normal are very frequent, as may be easily seen by close observation of this region during hernia operations. The tendon is sometimes narrowed and poorly defined, or entirely absent. In this case the fibers of the internal oblique and transversalis pass directly inward toward the edge of the rectus without forming any tendinous union. The lower portion of the muscles as they pass inward will be often found much thinner than normal, and there may even be spaces between some muscle bundles exposing the transversalis fascia beneath. Thus there is formed a triangle whose apex is at the internal ring, the sides being formed by the internal oblique and transversalis muscles and Poupart's ligament respectively, and the base by the edge of the rectus. The floor of the triangle is formed by the transversalis fascia. The area is a very weak spot in the abdominal wall, for it is covered, and but partially so, by the fascia of the external oblique."

Hessert believes that in cases with deficient tendon there will be found other evidences of maldevelopment, such as an atrophic condition of the fascia of the external oblique. This structure is sometimes very thin, almost transparent, and, in the region of the external ring, the fibers split up and separate so as to form an abnormally large opening.

Hessert considers it justifiable to operate on both sides in patients with a fully developed hernia on one side and a weak groin on the other. He states that where this was not done, he has had patients come back after several years with a real hernia on the other side.

I agree with Hessert that it is wise, particularly in children, to operate on both sides in cases in which there is a hernia on one side and either a markedly enlarged ring or exaggerated impulse on the other. In all these cases, with very rare exceptions, I have found a distinct peritoneal sac extending a longer or shorter distance into the canal and sometimes into the scrotum. I agree also with Hessert, that the development of a direct hernia is favored in those cases in which the conjoined tendon is either absent or poorly developed. As to the bearing of such absence of the conjoined tendon upon operative technique, Hessert believes that the technique best adapted for this condition is the imbrication operation of Andrews. In cases in which the triangle is especially large, he recommends utilizing the rectus muscle by incising the sheath, according to Bloodgood's technique.

Personally, I believe that when the typical Bassini is insufficient to effect a firm closure, the best method is to utilize the rectus muscle by one of the various methods that have been advocated. The best I believe to be that advocated by Wm. A. Downes.<sup>1</sup>

Hessert concludes that:

<sup>1</sup> Annals of Surgery, 1911, vol. lii, p. 568; already described by me in Keen's Surgery, vol. iv, and briefly reviewed elsewhere in this article.

1. The conjoined tendon is deficient or absent more often than has been generally observed.
2. This anomaly supplies an important predisposing factor in the development of direct herniæ, and probably plays a certain role, though a minor one, in the etiology of oblique herniæ.
3. The presence of this defect precludes the performance of the typical Bassini operation, except possibly in children.
4. The Andrews imbrication operation best fulfils the indications, regardless as to whether the tendon is absent or present. The Bloodgood transposition of the rectus will be found useful in certain cases.

**Strangulation of the Undescended Testis.** Farr,<sup>1</sup> of New York, has written an admirable paper on the strangulation of the undescended testis, with a very complete bibliography of the subject. He states the first recorded case is that of Delasiauve, in 1840. Nicoladoni, in 1885, reported 2 cases of his own and several from the literature. Farr states that the number has increased so that at the present time there are 150 recorded cases. In one-third of these cases there was an undescended testis, in a considerable portion of the remainder there was evidence of maldevelopment of some type.

Farr states that torsion of the cord cannot be produced in the normal human cadaver. The great majority of cases are strangulated by torsion, either of the testis on the epididymis; the epididymis on its own axis, or, by far the most often, the testis and epididymis upon the cord. This latter condition, he states, may occur within the tunica vaginalis, or, very rarely, without it, in which case the tunie and testis are both strangulated. Farr states that while strangulation may occur at any age, it is most common during the ten years immediately following puberty, and may affect either testicle. Untreated, it leads to aseptic gangrene, abscess, or simple atrophy. In animals, the gland is completely lost after twenty-two hours of strangulation, while in man 75 per cent. of the cases have had to be castrated, and, of the remainder, nearly all sloughed or atrophied. One has to bear in mind, he says, that in the case of the undescended testis one is dealing with a gland which is frequently abnormal and has already undergone degenerative changes. In strangulation by torsion, the conditions usually found are:

1. A free-lying testis, like an ovarian cyst on its pedicle. If the twist is of the testis proper, the true mesorchism or vascular pedicle of the testis must be abnormally long. If the testis and epididymis turn upon the cord, the mesoepididymis must be long and covered on each side with reflections from the tunie. More often the testis and epididymis hang free on the cord, like a ball on a string. In this case, the mesorchium is said to be absent, but, more properly speaking, it is abnormally long.

2. The relative size and position of the testis and epididymis vary greatly, the latter lying above, below, and even in front of the testis

<sup>1</sup> Annals of Surgery, December, 1913, p. 838.

after the twist is reduced. The two may be quite separate, with separate portions of the cord leading to each. The testis may be flattened and abnormal in shape and position, as is the epididymis also.

3. The tunica vaginalis is usually well-developed and capacious, frequently containing fluid and usually communicating with the general peritoneal cavity.

4. The cord may be abnormally short or long, is usually well developed, but may be flattened out and even divided into two distinct bundles, one containing the vas and its arteries, the other the spermatic vessels. In some cases no abnormality was present, and there was no apparent anatomic cause for the torsion.

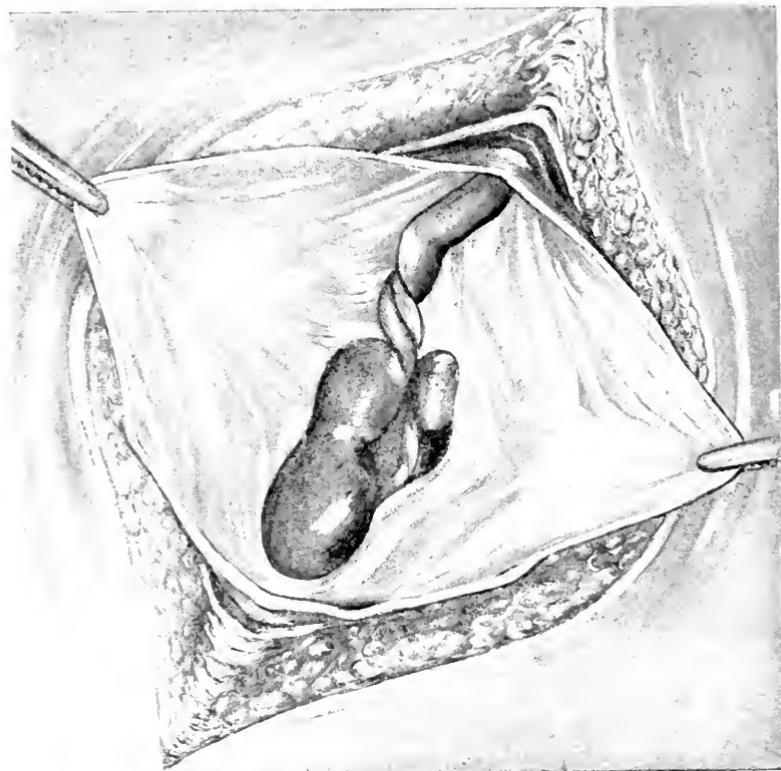


FIG. 10.—Necrosis of testicle from torsion of the cord.

As regards the mechanism of torsion, he states that each author seems to advance a theory to fit his own case. One writer believes that torsion is of slow development and that symptoms appear only after the last partial turn which completes the obstruction, a view which Farr does not share.

With the onset of torsion, great congestion ensues, accompanied

usually by a serous transudate, more or less sanguineous in character, into the tunica vaginalis. The increasing congestion dilates the veins, changing their length and thus again increasing the tendency to twist around the unchanged arteries and vas. The number of twists varies from one-half to four or more complete turns, averaging less than two. Curiously enough, the left testis usually, though not always, tends to turn clockwise, the right anti-clockwise. This may possibly be due to the pull exerted on the different elements of the cord, or to the natural tendency of the heavier and larger body of the testis to fall downward and outward toward Poupart's ligament as it comes through the internal ring. Supravaginal torsion must imply simply a very loose connection between the parietal layer of the tunic and the surrounding connective tissue.

Farr states, "the prognosis for the patient is always good, for the testis is nearly always bad, except in very early or very mild cases. The testes removed have all shown tremendous passive congestion, ecchymosis and subcapsular hemorrhages, with degeneration of the testicular substance, and varying degrees of necrosis, and even gangrene. Infection is rarely present."

Farr reports in detail a case in Dr. Wm. A. Downes' service at the Babies' Hospital, which he (Farr) operated upon in September, 1911; a second case operated upon by Dr. Frank Hartley, of the New York Hospital, in November, 1905; and a third case operated upon by Dr. Frank Mathews at St. Mary's Hospital, in October, 1911.

The last case can hardly be properly classed as true torsion, as operation disclosed no torsion at all, but merely stretching of the cord, and an undescended testis forced out of the external ring.

Farr reports 45 cases associated with undescended testis, and 7 other cases of maledescent.

Regarding the age of the patients, Farr's table shows that the same varied between three and a half months and forty-one years.

The greatest degree of twist was 1260, the lowest 180; the average twist in 33 cases was 480 degrees.

The correct diagnosis was rendered before operation in 14 cases; in 19, no diagnosis was made prior to operation.

The testicle was excised in 37 cases, saved in 4; it was saved, and then sloughed or atrophied in 2.

In conclusion, Farr reports a case in which a diagnosis of strangulated inguinal testicle, with possibly a Richter's hernia, had been made, and which, he states, "teaches the difficulty of excluding a strangulated hernia, and the folly of expectant treatment, as advised by some."

The patient, a boy, aged seventeen years, had been always well until a year previously, when the parents first noticed that the right testis was not in the scrotum. He had been playing see-saw and complained of great pain in his right groin where a small lump was noticed. The

pain passed away but returned at intervals. Following excessive climbing, the boy was taken with excruciating pain in the right groin in June, 1913, and admitted to St. Mary's Hospital. Bowels had moved regularly up to the last day. A tender lump was felt in the right groin. During a 30 mile trip in an automobile, he vomited three times. Examination at the hospital showed a healthy looking boy, no evidence of shock. No distention; temperature 99°, pulse 90. Left testis normal, right scrotal sac empty. In the right groin at the external ring, an exceedingly tender lump the size of a pigeon's egg, slightly movable, giving no impulse. At the level of the internal ring, a slight elevation was noted, extending along the canal. Operation seven hours after onset of symptoms. Usual Bassini exposure. The tumor at the external ring was found to be a tightly strangulated loop of ileum, containing hard feces and caught by the external ring. This was freed, examined and reduced. The testis was found at the internal ring, atrophic, misshapen, showing no evidence of torsion or other injury. The Bevan operation was performed and the child made a perfect recovery.

In the *Beiträge z. klinische Chirurgie* (Band lxxxvii, Heft 2, 1913), Flesch calls attention to the fact that formerly many cases of torsion were classed as *incarcerated inguinal testicle*, and that, hence, only a comparatively small number remains in which the diagnosis of incarcerated inguinal testicle seems to have been justified. Kocher has known of only nine such cases.

Flesch reports one case of descending incarceration of the inguinal testicle observed at the Frankfurt clinic in which, seven hours after the onset of circulatory disturbance in the testicle, due to incarceration, destruction of its function could be determined. The patient, a man, aged twenty-four years, gave a history of always having had an empty right scrotum, but that since adolescence he had noticed a slowly growing nodule in the right inguinal region, painful on deep pressure. A physician had pronounced the swelling a hernia and ordered a truss which the patient had worn for some years. On October 7, 1911, while at work lifting a heavy box, he suddenly felt intense pain in the inguinal nodule followed by vomiting. He had to be taken home in a carriage and as the symptoms rapidly increased, he was sent to the clinic, where, after careful examination, the diagnosis of incarcerated inguinal hernia was made. Immediate operation was performed; incision was made over the most prominent part of the swelling parallel to Poupart's ligament. After incision of the aponeurosis of the external oblique, a mass resembling a hernial sac appeared. This was incised and one to two tablespoonfuls of serosanguinous fluid evacuated. The cavity further contained an easily recognizable discolored testicle. The lower pole of the organ was wedged tightly within the external inguinal ring, and surrounded by the same in such a way as to render development most difficult. The cord, after incision of the vaginal sac, was followed up to the internal

ring. It was of normal consistence. It was divided, the proximal end ligated and buried in the abdominal cavity. The distal end, together with the testicle, was removed. Treatment of inguinal ring same as in castration. Suture of the internal oblique to the ligament, fascial suture of external oblique, suture of skin; primary union.

Flesch states that descending incarceration of the testicle may result in two ways, *either* as it did in the case of Quervain, in which a retained testicle, owing to increased abdominal pressure, was forced out of the external inguinal ring and could not return owing to increase in its size due to venous hyperemia, and became necrosed; *or*, incarceration takes place, as in the case above described, and—apparently also in a case reported by Godlee, as a result of great exertion of all abdominal muscles, the ectopic testicle being forced directly into the external ring and there retained.

In view of the severe shock that fairly characterizes these cases, as also the relative frequency of inguinal testicle (Lanz found 5 cases of retained testicle in 750 recruits examined by him), Flesch believes, with Kocher, that an inguinal testicle should be removed just as soon as it causes trouble.

I cannot agree with Flesch and Kocher that the inguinal testicle should be removed as soon as it causes trouble, unless by this is meant as soon as it becomes strangulated. One must not get the idea that the condition is a common one. During the twenty-three years of my connection with the Hospital for Ruptured and Crippled, at which place we have observed nearly 5000 cases of hernia, there has not been a single case of strangulation of the testis. In practically all of the ordinary cases of inguinal testicle, it is possible to bring the testis into the scrotum by operation, and I do not believe it should be sacrificed except in cases of actual strangulation. In other words, I would not wait until the testicle becomes strangulated, but advise an earlier operation which will accomplish a cure of the hernia which practically always accompanies the condition, and enable one to bring the organ down to its normal position in the scrotum.

Hanusa<sup>1</sup> discusses the **method of artificial synorchidy** as brought out by Mauclaire, in 1902, and later extended by him. The various steps of Mauclaire's operation are stated as follows:

1. Attending to the hernia.
2. Mobilization of the cord.
3. Division of the scrotal septum.
4. Incision of the tunica vaginalis propria of the healthy testicle.
5. Rhomboidal freshening of the albuginea of both testicles (see illustration).
6. Suture of the symmetrical borders of the freshened wounds of the albuginae.

<sup>1</sup> *Beit. z. klin. Chir.*, 1913, Band lxxxvii, Heft 2.

7. Enveloping both testicles by suturing together the tunica vaginalis plus remnant of hernial sac.

This completes the artificial synorchidy.

8. Suture of tunica vaginalis communis.

9. Suture of the deep tissues around the cord in order to fasten it.

10. Suture of skin with or without drainage.

After testing the method upon dogs, Mauclaire used it in nine patients, only five of which he had an opportunity to reëxamine three years later, and found the results, as regards location and size of the testicle, satisfactory.

He believes artificial synorchidy indicated.

1. In cases of cryptorchism (improvement of position, increased nutrition).

2. In varicocele (increased nutrition, disappearance of pain).

3-5. Division of vas deferens, loss of epididymis; obliteration of the vas deferens of the epididymis.

6. Cysts of the epididymis.

7. Unilateral sterility.

Later, Mauclaire added the complete division of the tissues of the cord. He had previously, in 38 cases of tuberculous epididymis, treated by removal of the diseased organ, divided the cord, without observing complete atrophy of the testicle in a single case.

In a case of bilateral cryptorchism in which Mauclaire was unable to guide the left testicle into the scrotum, he divided the entire cord. The right testicle could be brought down satisfactorily. The result, three months after operation, was good. The left testicle is said to have slightly decreased in size. The extended method was performed four times by Mauclaire with satisfactory result in every case.

At the Kiel Surgical Clinic, 39 cases of cryptorchism were observed between April, 1907, and December, 1912, 23 of which were operated upon by the method of Mauclaire slightly modified, as shown in the accompanying illustrations (Figs. 11, 12, 13, and 14); 9 according to Villemin, simple fixation; 3 according to Helferich; in 3, castration was performed; 1 not operated upon.

Hanusa gives a comparative table of the results of the various methods as regards size, consistence, and location of the testicle; and, on the basis of the same, states that absolute superiority cannot be claimed for any one of the methods. The table shows that in 3 of 8 cases operated upon by Mauclaire's first procedure, the position of the testicle was ideal; in five others, almost ideal. In 4 cases operated upon by Mauclaire's extended method, there were three ideal and one almost ideal result. In 3 cases operated upon according to Villemin, the position of the organ was ideal in 3. In 6 cases operated upon according to Helferich, the testicle had retained an ideal position in three, while in the other three it had slid upward.

Hanusa's conclusions are (1) that Mauclaire's operation for retained testicle, clinically, does not seem to offer any advantages over other methods either as regards increase in size of the testicle, change in consistence, or improvement of position. (2) That in view of the experience of Bevan, Mosehowitz, and others, there is no *raison d'être* for artificial synorchidy according to Mauclaire, which is supposed to bring about better nutrition of the transposed testicle, since the arteria deferens, in consequence of its anastomosis with the spermatica, is capable of furnishing the desired nutrition. That a communication between the seminal vesicles does not occur, is shown by Martini's experiments. (3) To attach a mal-descended testicle to a healthy one in order to keep it in position, becomes unnecessary since, after division of the vessels of the cord, the retracting power is no longer present. I fully agree with Hanusa that the good results following the operation of Bevan leave little ground for advocating the procedure advocated by Mauclaire.

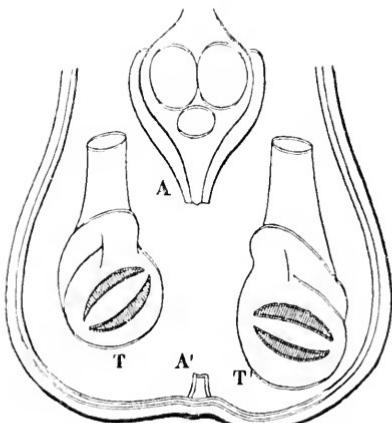


FIG. 11.—*A* and *A'*, region or resection of the scrotal septum; *T*, ectopic testicle; *T'*, normal testicle.

**Ectopic Testicle.** Gundermann,<sup>1</sup> of Witzel's Clinie, in his article on "Perineal Ectopic Testicle," states the following two conditions which must be fulfilled in cases of ectopic testicle: (1) The testicle must have left the peritoneal cavity (inguinal canal). (2) It must be located at a place where it is never found in the entire course of its normal descent.

In *true* crural ectopia the testicle passes through the aperture through which normally the vessels pass (lacuna vasorum), below Poupart's ligament, and becomes palpable in the upper portion of the thigh. These cases are exceedingly rare and should not be confounded with

<sup>1</sup> *Beit. z. klin. Chir.*, 1912, Band lxxxii, Heft, 1.

*false ectopia*, in which the testicle in reality is retained in the inguinal canal, but in consequence of weakness of the aponeurosis of the external oblique, becomes located in front of the crural ring.

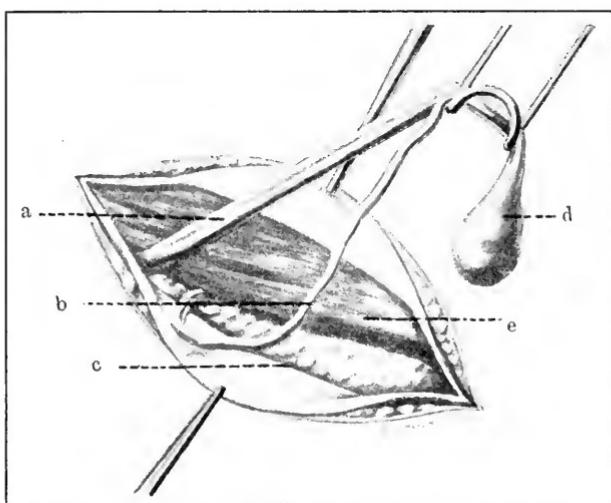


FIG. 12.—*a*, vessels of the cord; *b*, vas deferens; *c*, Poupart's ligament; *d*, testicle; *e*, internal oblique muscle.

Inguinal perineal ectopia, he states, is not quite as rare as true crural ectopia. It is usually unilateral, and seldom complicated with a hernia.



FIG. 13.—*a*, right testicle; *b*, left testicle; *c*, anterior suture of albuginea.

Gundermann reports a case of perineal ectopia associated with hernia, observed in an infant, ten weeks of age, the condition having existed

since birth (Fig. 15). The operation was performed by Witzel, and, in connection with the same, Gundermann discusses the question of the origin of this type of ectopia. He states that no remnant of the gubernaculum extending toward the scrotum could be found, and the testicle, which was situated in the fundus of the hernial sac, could be easily pulled forward; there were no adhesions, nor was there any bulging

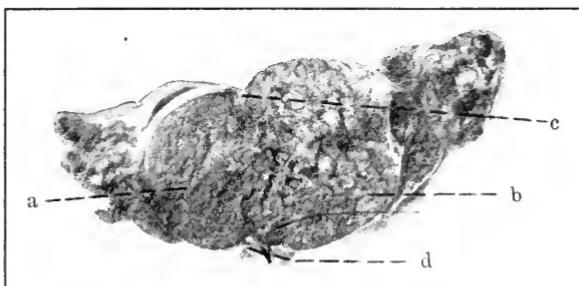
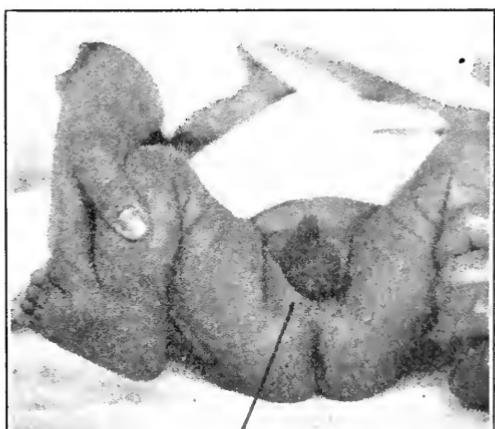


FIG. 14.—*a*, right testicle; *b*, left testicle; *c*, posterior suture of albuginea; *d*, anterior suture of albuginea.

of the hernial sac in the direction of the scrotum, all of which points he considers important factors in connection with the evolution of ectopia. He carefully reviews the normal descent of the testicle, and states his belief that perineal ectopia is never the result of a retention. On the other hand, he believes that a retained testicle may pass into the perineum long after birth.



Testicle.  
FIG. 15

On a basis of a careful study of the subject, he concludes that ectopia testis perinealis is a subtype of ectopia processus vaginalis perinealis. This occurs as a primary internal anomaly and may possibly represent

an atavistic formation. Furthermore, he considers it probable that a fetal peritonitis may bring about a perineal direction of the vaginal process. A connection between perineal ectopia and retained testicle does not exist beyond the fact that both anomalies are due to the same cause, but perineal ectopia is never the consequence of a retained testicle.

Whether or not the position of the fetus during the last months of pregnancy has any direct or indirect influence upon the direction of the vaginal process, has not yet been determined.

He further states that the question as to whether a primary false insertion of the gubernaculum occurs in these cases, still remains undecided.

In my paper on THE TREATMENT OF THE UNDESCENDED OR MAL-DESCENDED TESTIS ASSOCIATED WITH INGUINAL HERNIA, published in the *Annals of Surgery*, September, 1908. I stated that:

Perineal ectopia, although described by Hunter in 1786 and afterward by Curling in 1841, has received very little attention by surgical writers since. Curling was the first to give a detailed description of the condition in 1857, and a report of 9 collected cases. He was also the first one to treat the condition by operation. The patient was an infant four weeks old. The result of the operation was unfortunate.

Godard, in 1857 and 1860, reported two interesting cases, one a man, aged fifty-six years, another of twenty-two. The first case was originally an inguinal ectopia which, after having worn a bandage for a considerable time, became perineal; the second case was a cruroscrotal ectopia.

My own statistics show 9 examples of perineal ectopia in 126 cases of hernia with undescended or maldescended testis operated upon.

At the Hospital for Ruptured and Crippled there have been observed during the past eighteen years 737 cases of undescended testis, and of these only 15 were of the perineal type. In 6 no operation was performed.

*Etiology.* Authorities differ widely as to the precise cause of the descent of the testis into the perineum. Until recently there was a tendency to accept fully the opinion of Curling that had become almost classic, that the principal and almost only agent connected with the descent of the testis was the gubernaculum; and as the latter was admitted to have several fasciculi, one attached to the lower part of the scrotum, another extending into the perineum to the margin of the ischium, and a third into the pubic or femoral region, this seemed an easy and sufficient way of accounting for the different types of maldescent of the testis. In the perineal variety the fibers were supposed to be more fully developed than in the inguinal type, and by traction the testicle became lodged in this region.

Godard accepted the theory fully and believed nothing more simple than this explanation—no gubernaculum and the testis remains within the abdomen; no middle fasciculus, and inguinal ectopia occurs, while

in the event of the anomalous insertion of the fasciculus either in Searpa's triangle or the ischium, we have cruroscrotal and perineal ectopia.

Lockwood believes the gubernaculum the main factor in the descent of the testes, and attributes the various types of maldescent to over-development of portions of the gubernaculum lying in these particular regions. He states: "The muscular structure of the gubernaculum is, I think, unquestionable, and it seems irrational to deny its tissues their function, namely, that of traction." He regards it of special significance that, in case of maldescent, the testicle migrates into particular regions in which, as has been well established, the fibers of the gubernaculum exist. I do not believe that Lockwood's argument is entirely convincing.

Later, Sébileau, after careful personal research upon the coverings of the testicle and its migration, concludes that "perineal ectopia is a purely congenital affair. It depends neither upon pathological nor anatomical causes and least of all upon the gubernaculum." He recognizes that the absence or insufficient development of the gubernaculum may explain abdominal and iliac retention. As regards the inguinal and extra-inguinal retention, he believes that the abdominal wall itself plays a very real and important role in offering difficulty to the complete passage of the testicle through the external ring.

My own experience leads me to accept the views of Sébileau, that perineal ectopia is of congenital origin, and nearly always associated with a hernia.

Schrager,<sup>1</sup> of Chicago, expresses his views as to the MECHANISM OF THE SACS IN BILOCULAR HERNIA. He states that in his search through the literature, he has found not a single case similar to Dr. D. D. Lewis' case recently operated upon at the Presbyterian Hospital of Chicago.

Schrager states that, "by bilocular or multilocular hernial sacs, we understand the presence of two or more sacs in the same inguinal or femoral hernia, the pouches communicating with one another. Properly speaking, a double sac is merely a division of one sac. As B. Schmidt<sup>2</sup> puts it: There are no double or multiple sacs, just as there is no absence of the sac. Sac made up of several concentric layers, like the leaves of an onion, were described by several of the older writers. Dieffenbach, Gunther, and Pitha, among others, described sacs with 8 to 10 concentric layers. This type of sac is not included in our description." He believes that all the hitherto described types of bilocular hernia can well be covered by the term interparietal herniae. They have many features in common. A large majority of herniae of this type are associated with undescended or maldescended testis. The illustrations accompanying the paper give a good idea of the character of the sac in the herniae operated upon by Lewis (Figs. 16, 17, and 18).

Schmidt<sup>3</sup> brings an article on "The Radical Operation for Enterocèles

<sup>1</sup> Surgery, Gynecology, and Obstetrics, April, 1913, p. 359.

<sup>2</sup> Deutsch Zeitschr. f. Chir., vol. xlvi, p. 129.

<sup>3</sup> Ibid., May, 1913.

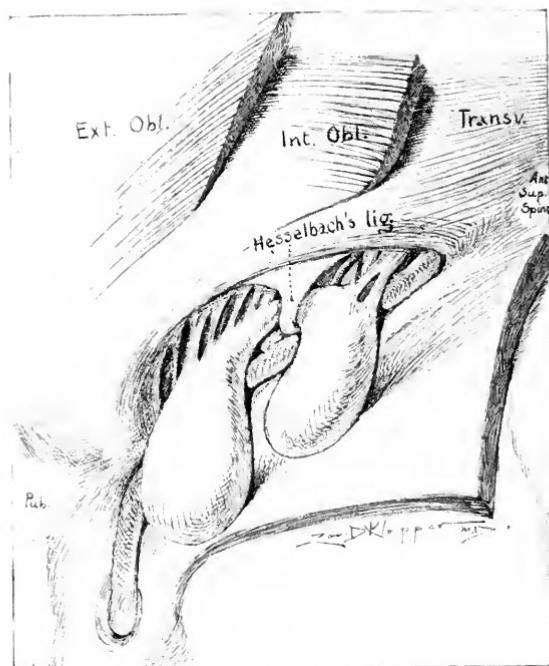


FIG. 16.—Biloculation of a hernial sac by a strongly developed Hesselbach's ligament.

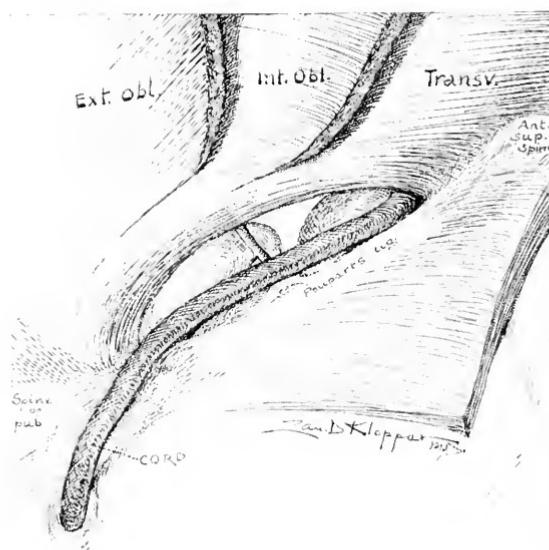


FIG. 17.—Showing Hesselbach's ligament.

with Incomplete Sac (Sliding Hernia)," and reports three personal cases. He refers to the valuable treatise on the subject by Sudeek, and quotes from the latter's operative description as follows:

"At the time of opening the sac the trouble begins, all the more as the hernial portion of gut sometimes has become twisted around its own axis, and its posterior aspect, which is without peritoneum, has become turned to the front. One has to be very careful, therefore, not to attack the lumen of the gut instead of the sac. Reduction of the gut can, of course, not be accomplished in the usual way, inasmuch



FIG. 18.—Double hernia sac.

as it cannot be loosened from the sac. The gut therefore must be replaced *en masse*, together with the sac. For this purpose the opened sac is temporarily closed again after examination of conditions. The hernial sac, plus intestine, is completely separated from the surrounding tissues; great care has to be exercised not to cause any unnecessary injury to the vessels, as such may not only lead to hemorrhages but may jeopardize the nutrition of the gut. After this, the entire hernial sac plus contents is replaced and held by a firm canal suture. In a small number of cases in which it was found impossible to loosen the sac

from its adhesions, resection of the gut became necessary. In all operations for sliding hernia, large incisions, broad opening of the sac, if need be by means of hermiolaparotomy in Trendelenburg's posture, are recommended."

For the purpose of finding the lumen of the sac without causing secondary injury to the gut, Schmidt recommends a procedure which has been of service to him in his operations. It consists in taking a fold of the sac between the thumb and forefinger and rolling the two sides of the fold upon each other in order to ascertain whether or not the respective portion is free from gut. In elucidation of what Sudeck means by "reduction *en masse*," Schmidt submits the accompanying drawings. Fig. 19 shows the hernial ring above, from which the sac is

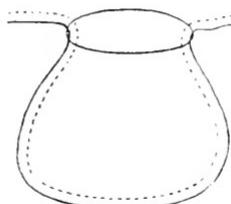


FIG. 19

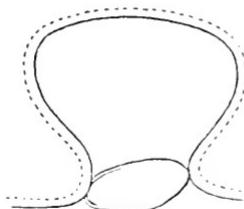


FIG. 20

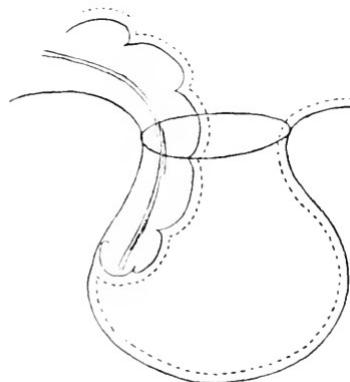


FIG. 21

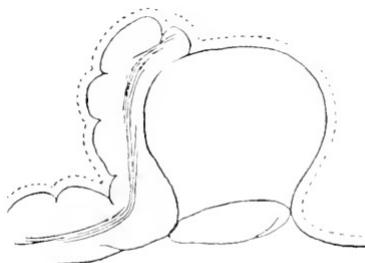


FIG. 22

suspended. The uninterrupted line represents the retroperitoneal surface; the dotted line, the peritoneal surface of the sac. Fig. 20 shows conditions after reduction, a "diverticulum" having been changed into an "inverticulum." The conditions in a case of a sliding hernia of the cecum—colon ascendens—are demonstrated by Figs. 21 and 22. Fig. 21 is supposed to represent a hernial sac (right side) in the lateral angle of which the large intestine has become adherent to the wall of the sac. Fig. 22 shows the result of "invagination reduction."

Schmidt gives a résumé of his findings, as follows: (1) In sliding

hernia of the large intestine *right* side, one has to deal with half a loop of gut; on the *left* side, with an entire loop (rare exception on right side being an entire loop (rare exception on right side being the "rocking hernia" = "herniae par bascule"). (2) The practice of rolling a fold of the sac between the fingers, helps one in finding a portion of the sac that is free from gut. (3) Reduction of the sac of a sliding hernia, after it is shelled out of its covering, is accomplished by inversion, no matter whether the sac was incised and closed again, or remained unopened. (4) Protruding parts of the hernial sac should be resected before reduction. Such parts, however, as may contain vessels feeding the gut, should be carefully preserved. To determine this it may be well to hold the sac up against the light. (5) Special propositions for the resection of the sac in special forms of sliding hernia are:

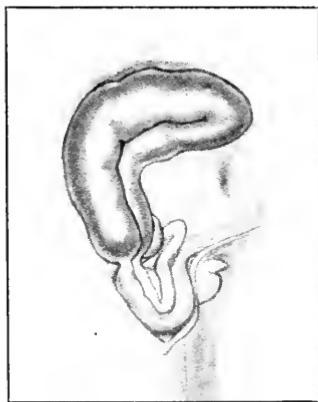


FIG. 23

(a) In cases of isolated sliding hernia of the appendix, appendectomy should be done and the sac removed *in toto*.

(b) In sliding hernia of the ileum, the sac should be amputated below the gut.

(c) In sliding hernia of the large intestine on the left side, the loop formation of the gut should be carefully noted; such parts of the sac as are lateral to the convex border of the loop may be resected.

(d) The mobilization of such parts of the colon as resist reduction may be facilitated by splitting the abdominal coverings from the external angle of the hernial opening outward and upward. The upper (right efferent, left afferent) parts of the colon are thus loosened from the ileum which carries them, and made more flexible or elastic.

(e) When it is difficult to separate the cord from the sac, the feasibility of implanting the testicle in the abdominal cavity should be considered instead of castration.

In an article on the subject of "Retrograde Incarceration of the Gut

in Hernia," Wistinghausen<sup>1</sup> enters rather fully into the question of the development of these herniae. He cites three possibilities:

1. Retromigration.
2. Reduction.
3. Hernia of the intestine; double, triple, etc.

As regards No. 1, he assumes that the gut itself, owing to gases and peristalsis, is induced, under certain conditions, to start on a retrograde course (Fig. 23). As to the second possibility mentioned, he assumes

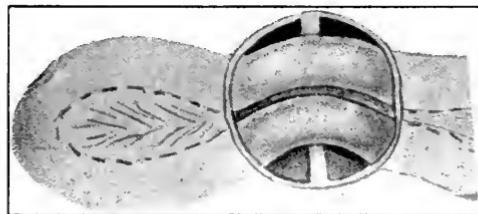


FIG. 24

that the condition in question may develop as a result of reduction maneuvers undertaken at a time when complete incarceration had not yet taken place, but a rather long loop of intestine had passed into the large hernial sac.

The third causative possibility suggested by Wistinghausen is, that two or three loops pass into the sac either at the same time or following one another.

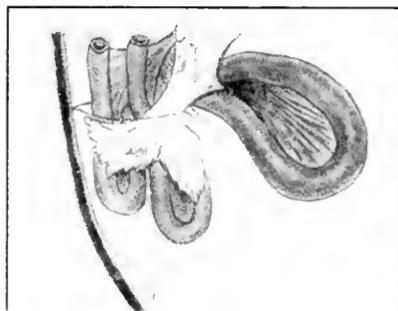


FIG. 25

There are cases, however, he states, in which the gut must have passed into the sac through one opening in the abdomen and slid back through another (see Fig. 24, case of Lorenz). Such cases prove that the gut is capable of emerging from a hernial sac and partly return into the abdominal cavity through a fissure in the hernial opening. The propelling force in these cases he supposed to be peristalsis rather than gases in the gut.

<sup>1</sup> Deutsch. Zeitschr. f. Chir., May, 1913.

He cites a case of Sultan's (Fig. 25) in which the middle loop was adherent to the hernial opening as well as the omentum; it could not, therefore, nor could its mesentery, have been within the sac.

Wistinghausen concludes on the basis of his studies (1) that incarceration of the mesentery is brought about by the fact that the connecting loop passes the hernial ring twice; in so doing it becomes distended to such an extent that under favorable conditions it may pull out of the sac not only the mesentery, but even the hernial loops. (2) In the event of a prolapse of two loops of small intestine, the connecting loop is not materially damaged and this form does not represent a retrograde incarceration. (3) That it is difficult to say just what role attempts at reduction may play, that they should, however, be avoided whenever there is suspicion of retrograde incarceration or hernia duplex.

Wistinghausen states that he found retrömigration to be a more frequent occurrence than prolapse of a number of loops. Of the former, he collected 41 cases; of the latter, only 23.

Alexander,<sup>1</sup> of Philadelphia, gives a detailed report of 105 cases of strangulated hernia operated upon at the Episcopal Hospital during the past six years. He states that the mortality of strangulated hernia remains about as bad as what it was ten to twenty years ago. He adds that it will be unrelieved, an acute, progressive, abdominal condition, and the mortality will remain unchanged until the profession and public, as in appendicitis, and as we are trying to do in cancer, become better educated to the fact that an early operation and the avoidance of taxis in herniae are the two most important factors in lessening the mortality.

Of the 105 cases of strangulated hernia, 58 were males and 47 females, 60 were inguinal, 25 femoral, and 20 umbilical.

The mortality of inguinal hernia in the male was 23 per cent., in the female 50 per cent.; femoral hernia in the male 50 per cent., in the female 26 per cent.; umbilical hernia in the male 25 per cent., in the female 50 per cent. The total inguinal mortality, male and female, was 26 per cent., femoral 28 per cent., umbilical 45 per cent. The total male mortality was 24 per cent., the female 38 per cent., and the male and female together 30 per cent.

The lowest mortality was noted in a group of 8 cases between twenty to thirty years of age, with no deaths; in 6 cases between one to ten years there was one death; in 7 cases between fifty to sixty there were 4 deaths, while in 10 between seventy and eighty, there were but 2 deaths.

The ages of the patients ranged between six weeks and eighty years; the duration of the hernia from two weeks to sixty years. The most constant symptoms of strangulation were sharp pains at the hernial orifice, colicky pains, nausea, and vomiting.

<sup>1</sup> Annals of Surgery, November, 1913.

Alexander states that simple taxis, or taxis aided by an anesthetic, morphin injection, local application, hot bath, elevation of the foot of the bed, etc., often prolongs the question of operative interference for hours or days. So important was the question of taxis and so dangerous its use, that the old surgeons tried to place a limit of time, varying from a few minutes to two hours, during which it was safe to persist in its use.

I do not consider it wise to continue taxis for more than five minutes, nor do I believe that taxis should be attempted at all in the cases in which the symptoms of strangulation have been exceedingly severe from the start, nor in those in which strangulation has occurred in previously irreducible hernia, nor in cases in which twenty-four hours have elapsed after strangulation.

Ether, according to Alexander, should be the anesthetic of choice in the majority of cases, preceded in advanced cases or those associated with fecal vomiting, by washing out the stomach. Local anesthesia is advised in cases complicated by cardiorenal and lung conditions. Its disadvantages are the increased length of time required to perform the operation and the mental shock often accompanying it. Spinal anesthesia he believes to be a dangerous anesthetic, even in the hands of an expert.

In this view I fully concur. Unless absolutely contra-indicated, he adds, ether is certainly the anesthetic of choice, and is not complicated by pneumonia or uremia any more frequently than any of the other anesthetics mentioned.

With regard to the operation, Alexander believes resection to be the ideal procedure, provided conditions are favorable. But, in most cases, the physical condition of the patient may warrant only relieving the constriction. In large scrotal and umbilical herniae, on account of the many and dense adhesions, it is often best to simply relieve the constriction.

One of the most remarkable recoveries in Alexander's series was seen in a woman, aged fifty years, with a femoral hernia involving the small intestine which had been strangulated for four days. An artificial anus was established, which later healed spontaneously.

In strangulated herniae of the Richter type, or partial enterocoele, either femoral or inguinal, the mortality is high. This is probably due to the fact that they are small and often overlooked, and consequently come to the surgeon late. In this type, on three occasions the hernia reduced itself while the patient was being anesthetized. In the first case, a herniorrhaphy was performed without exploring the gut; the patient died in two days of a diffuse peritonitis, and the autopsy showed a perforated gangrenous area the size of a penny. In the other 2 cases, at the time of operation, the gut was caught and pulled down into the wound, thus enabling the operator to ascertain the true condition of affairs.

The cause of death in Alexander's 32 fatal cases was as follows: Peritonitis, 11; uremia, 3; pneumonia, 4; shock, 5; myoendritis, 2; delirium tremens, 2; apoplexy, 2; acute dilatation of heart, 1; volvulus, 1; sarcomatosis, 1. He adds that the 5 cases that died of shock were desperate ones and really should be classed as due to peritonitis.

In order to improve the statistics of strangulated hernia, or rather, prevent the occurrence of this condition, Alexander makes a strong plea that all simple herniae in children, especially those of the scrotal type, be operated upon. He believes it wrong to order a truss in these cases, as the percentage of cures is very small. Whereas, if a radical cure be performed in all cases in children, he states, a great step will have been taken toward the prevention of strangulated hernia.

In general, I agree with this view, provided it does not apply to infants or very young children. I still believe it is wiser to treat infants suffering from hernia by some form of mechanical support, preferably a Hood spring truss, provided the hernia is controlled by this means. In all cases, even in infants, in which there is danger of strangulation, I would recommend an operation. Attention should be called to the fact, however, that strangulation is comparatively rare in young children and, even if it does occur, operation can be done with little risk. At the Hospital for Ruptured and Crippled we have operated upon 32 cases without a death. If, after the infant reaches the age of three to four years, the hernia still comes down, even though very rarely, operation should be performed. If the hernia develops in childhood, or is first discovered after the age of four years, I believe it wiser to perform immediate radical operation.

**Hernia of the Adnexa.** Matthey<sup>1</sup> reports a case of *Incarcerated Hernia of the Adnexa*, in an infant three months old. The child, who had always been well, had a sudden attack of vomiting, and the next day, upon bathing, the mother observed a swelling in the inguinal region. The family physician made an unsuccessful attempt at taxis. Vomiting was repeated; no stool was passed for thirty-six hours. Examination at the Wiesbaden clinic showed a hard, ovoid tumor, the size of a hen's egg, one finger's width above Poupart's ligament, passing in the direction of the labium majus; the skin was intact. The tumor was entirely irreducible and gave a dull sound on percussion. A diagnosis of incarcerated inguinal hernia was made. Evacuation of stool occurred on the operating table. An incision was made parallel to Poupart's ligament, following the longitudinal direction of the tumor. Upon splitting the aponeurosis, a dark-colored hernial sac, the size of a pigeon's egg, came into view. The same could be easily isolated; it had a hard, narrow neck. On opening the sac, a small amount of black fluid escaped. A hard, bluish-black, kidney-shaped tumor accompanied by a cord, the

<sup>1</sup> Beitr. z. klin. Chir., 1913, Band lxxxi, Heft 2.

thickness of a pencil, became visible. The ovary lay in front of the tumor. Slight pulling brought the horn of the right uterus to the surface; there was no torsion of pedicle and no sharp incarceration. Resection of the adnexa close to the uterine horn was performed, as recovery seemed excluded. Then inversion of the stump below to the peritoneal folds of the ligamentum latum; the ligamentum teres could not be found, the wound was closed by layer suture; death occurred after four days.

With reference to the relative frequency of hernia of the adnexa, Matthey states that Hilgenreiner found but seven in a series of 2238 cases. Other authors record a larger proportion. Every age seems to be represented. According to Puech, more than half of the cases are of congenital origin (54 out of 85). Matthey states that, inasmuch as a large percentage of these herniae are diagnosed only after incarceration, or in the presence of some other complication, their frequency is probably far greater than is generally believed.

Damianos disapproves of the classification of "congenital" and "acquired" hernia of this type, claiming that the herniae themselves are never congenital but only the sac.

Matthey states, that they have often observed, when operating for hernia in the female, not only when omentum or gut formed the contents of the sac, but also when the latter was entirely empty—that the sac had the shape of a tube, and the neck passed through a very narrow canal which speaks in favor of congenital predisposition.

It has been found that the right side is much more frequently affected than the left.

**Therapy of Incarcerated Hernia.** The September, 1913, issue of the *Deutsche Zeitschrift für Chirurgie*, contains an article by V. Gussew, "On the Therapy of Incarcerated Hernia on the Basis of 420 Cases" observed at v. Bergmann's Clinic at Riga, between 1902-1912 (281 being men, 139 women). 280 of the cases were inguinal hernia, 100 crural, 31 umbilical, 2 epigastric, 4 ventral, and 3 diaphragmatic hernia. Two-thirds of the cases had passed the fourth decade of life. The oldest patient was eighty-eight years, the youngest seventeen years. (None below fifteen are admitted.) 71 = 17 per cent. of the cases had been constantly wearing a truss; 27, or 6 per cent. of the patients, did not know they had a hernia until incarceration occurred.

The treatment of these incarcerated herniae was operative whenever possible, taxis being resorted to only in extreme cases. Spontaneous reduction was noted in 26 cases. 73, or 19 per cent. of the cases, had been previously treated by taxis, with dire results in many instances. A scrotal hernia was found in 2 cases, hemorrhage of the sac, reposition *en bloc* three times, accrete hernia twice, gangrenous gut in the sac was found 18 times, perforated gut in the sac, twice. 18, or 25 per cent. of the cases in which taxis had been employed, resulted fatally,

although in 60 per cent. of these cases operation was performed within forty-eight hours after incarceration.

As regards the method of operation, it appears that simple herniotomy was performed in 250 cases of inguinal, crural, umbilical, and ventral hernia, with a mortality of 12.4 per cent.

The normal procedure in gangrenous hernia was primary dissection of the gut, with circular suture or Murphy button for the anastomosis. The Murphy button was used in 69 cases, and Gussew states that its advantages were not apparent. In 37, or 53 per cent. of the cases, a fecal fistula resulted which ended in death in 21, or 57 per cent. of the cases, while of the 38 cases treated with suture of the gut, only 9, or 24 per cent., developed a fecal fistula, with a mortality of 88 per cent.

Of late, they have been giving lateral apposition the preference whenever the patient's condition permitted this, but the results have been more satisfactory.

Spontaneous reduction *en bloc* is reported twice, in one case the hernial sac was found properitoneally in the right iliac fossa. Incarceration in the internal inguinal ring was seen in 2 cases in addition to 6 already reported; 3 cases of interstitial hernia were observed, torsion of the omentum was noted twice, strangulation of the omentum twice, resection of omentum was done in 92 cases—in 18 of these, resection of the gut was added. The total mortality, in the 421 cases of incarcerated hernia reported, was 27 per cent. The mortality of the gangrenous cases was 57 per cent., and that of the non-gangrenous, 12.4 per cent.

Of 32 cases of enterocele, 10 died = 30 per cent. Of these, 11 were treated with resection of the gut (5 deaths), one with artificial anus. Of 23 cases of hernia of the large intestine, 9, or 39 per cent., ended fatally. The average duration of incarceration was three days. In the pure omental herniae, the mortality was *nil*.

"The Pathogenesis of Hernia of the Omental Bursa with Normal Hernial Opening" is the title of an article by Borscaky.<sup>1</sup>

He states that hernia of the omental bursa represents one of the rarest forms of herniae. It might even be questioned, he states, whether a condition in which a loop of intestine passes through either a normal or a pathological opening of the peritoneum into the omental bursa, a cavity fully lined with peritoneum, should be classed as a hernia, inasmuch as, according to accepted ideas as to what constitutes a hernia, the peritoneum should be pushed forward by a loop of intestine. However, the presence of an hernial opening and a peritoneal covering in these cases, justifies the designation "hernia."

Blandin, in 1823, proved by autopsy that the Foramen of Winslow may "play the role of a hernial opening." Jeanbrau and Riche could find but twenty-one such cases reported in the literature, and, since then, Borscaky has found but one other case, namely, that of Corwardin.

<sup>1</sup> *Beit. z. klin. Chir.*, 1912, Band Ixxvii, Heft 2.

Conditions which favor the development of these herniae are (1) a wide hernial ring; (2) dislocation of the aperture toward the linea alba. Furthermore, as regards the intra-abdominal organs, the complete absence, or but rudimentary development of the major omentum, enlargement of the minor omentum, elongation of the mesentery, elongation of the mesocolon.

Borscaky reports one case of hernia of the omental bursa, operated upon in 1910 at the Budapest Clinic, in which a convolution of small intestine had passed from the foramen of Winslow into the omental bursa. The case had been diagnosed as a duodenal ulcer. At operation, the loops of small intestine were found above the minor curvature of the stomach, and covered by the minor omentum. The gut forming the contents of the sac could be easily pulled forward. There were no signs of strangulation. After emptying the omentum, the foramen of Winslow was found to be wide open so as to easily admit two fingers. It was pushed markedly toward the median line. The appendices epiploicae were undeveloped. The stomach was found dilated and in an almost vertical position. The minor omentum was thickened, and a duodenal ulcer, for which the operation had been done, was found.

On the basis of a study of the reported cases, Borscaky believes that the duodenal ulcer caused changes in the borders of the foramen of Winslow, which facilitated the entrance of the loops of intestine.

**Rare Forms of Hernia.** Lincoln Davis,<sup>1</sup> of Boston, reports a recent case of *strangulated retroperitoneal hernia of the small intestines into the paraduodenal fossa*, in a man, aged forty-eight years, with a negative previous history up to six years ago, when he had an attack of acute abdominal pain lasting six days. He had been troubled since with gas in stomach and discomfort two or three hours after meals. He entered the Massachusetts General Hospital on July 15, 1913, at 2.40 P.M. The abdomen was full, markedly distended and tense, with loud tympany throughout. No dulness or signs of fluid were present; there was board-like rigidity of whole left side of abdomen. Immediate operation was decided upon. A four-inch median incision below the umbilicus disclosed a bulging retroperitoneal tumor the size of a football lying principally to the left of the median line and extending up to the epigastrium (see Fig. 26). The incision was enlarged above the umbilicus; the parietal peritoneum was incised, and there was an escape of considerable turbid, bloody fluid. The incision in the posterior parietal peritoneum was then enlarged and a large mass of distended, plum-colored, small intestine delivered. The point where the ileum emerged from the retroperitoneal pouch was found to be close to the point where the duodenum emerged from under the mesocolon leading to the left. The bowel was found adherent to the edge of the opening; these adhesions were freed. The remainder of the ileum and entire

<sup>1</sup> Boston Medical and Surgical Journal, February 19, 1914.

jejunum lay in the hernial sac. With considerable difficulty, the herniated intestine was pulled through the opening. The hernial ring could not be enlarged on account of large mesenteric vessels which ran close to its edge. No attempt was made to close the hernial opening on account of the alarming condition of the patient. The intestines were pressed back into the peritoneal cavity with difficulty, and the abdominal wall was closed with through and through sutures of silkworm gut. The patient returned to the ward in poor condition and failed to respond to stimulation, and died at 9.10 A.M.

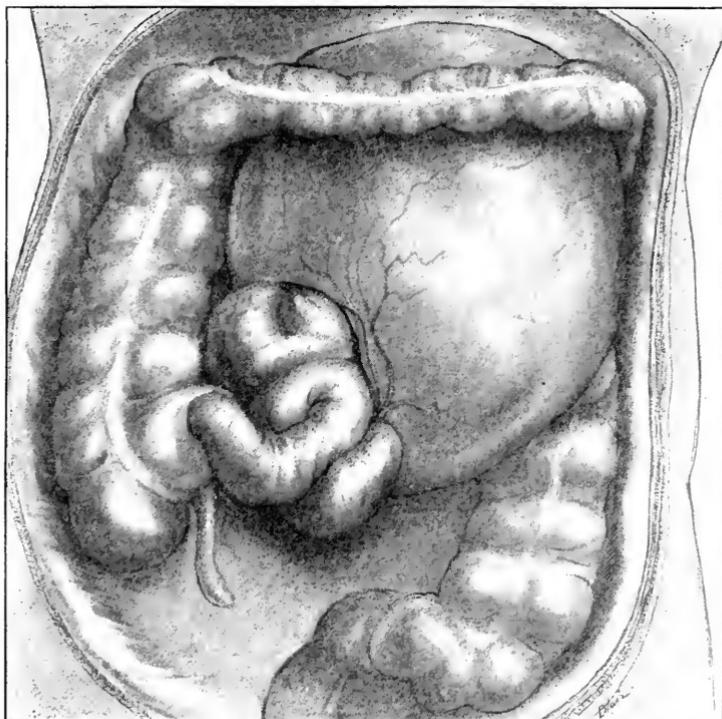


FIG. 26

Moynihan, in his monograph on retroperitoneal hernia, describes nine fossæ in relation to the duodenum: (1) A superior duodenal fossa; (2) an inferior duodenal fossa (fossa of Treitz); (3) a paraduodenal fossa (fossa of Landzert); (4) a mesentericoparietal fossa (fossa of Waldeyer); (5) a mesocolic fossa; (6) a posterior duodenal fossa; (7) a duodenojejunal fossa; (8) an intermesocolic fossa; (9) an infraduodenal fossa. The last four are very unusual fossæ. Moynihan records 65 cases of left duodenal hernia, and 17 cases of right duodenal hernia. These herniae are found at all periods of life, the youngest being the

case of Borscaky, in which the patient was fourteen days old. Moynihan believes that the hernia is often congenital, and states that under favorable circumstances it is possible to make a probable diagnosis during life.

Moynihan states, "so far as the symptoms of the hernia are concerned, there is little to be said. They may be slight or they may be the sudden symptoms of acute intestinal obstruction. In a number of carefully recorded cases, the history of chronic slight digestive or intestinal trouble is usually obtained. The treatment is operative. A number of successful cases have been recorded by Sonnenberg, Priestly, Leach, Narth, Knaggs, McArthur, and others, in left duodenal hernia, and Neumann in right duodenal hernia."

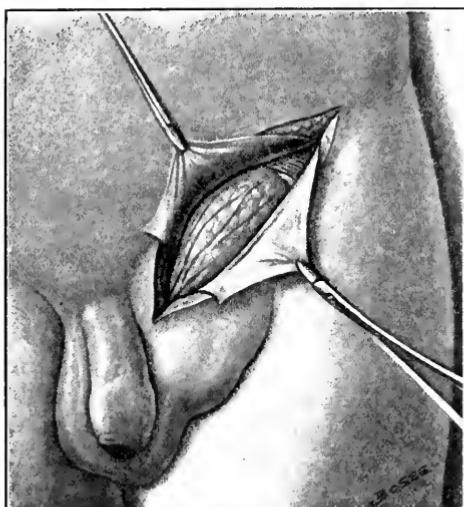


FIG. 27.—Incarcerated fat hernia, left inguinal canal.

In reviewing his case above briefly described, Davis states that the correct preoperative diagnosis should have been made, as all the signs of intestinal obstruction were present, together with a distinct, globular, tympanitic, tender tumor, lying on the left of the median line, high in the abdomen.

HERNIA ADIPOSA, OR FAT HERNIA, has been described by Friedman,<sup>1</sup> of New York. He states that little has been written about the subject for many years, and reports 2 cases illustrating the condition.

In the first case reported, I believe that the condition was something more than a mere fat hernia. A careful study of the conditions found, together with the later history, make it almost certain that it was a case of hernia of the bladder. In bladder hernia of the paravesical type, there is almost always present a very large amount of extra-

<sup>1</sup> Annals of Surgery, February, 1913, p. 204.

peritoneal fat which sometimes completely occupies the canal or even the upper scrotum, and in such cases the absence of a peritoneal sac would not be unusual. The statement that the mass was "densely adherent to surrounding structures, particularly at the external ring, as well as to the cord" confirms this opinion. Separation of these adhesions and the removal of the entire mass of fat very probably produced a contusion, or wound of the bladder wall. The fact that the patient passed bloody urine on the second day, and died of total suppression on the fifth, seems to support this view.

The second case was a "lipoma of the inguinal canal with a true hernial sac present." "To the fundus of this sac a pyriform-shaped piece of fat, filling the inguinal canal, the size of a hen's egg, was attached, undoubtedly causing a weakened canal and large external ring" (Fig. 27).

The condition described has not been, in my own experience, very rare. I would hardly designate it as a fat hernia, inasmuch as the presence of a larger or smaller amount of extraperitoneal fat might be regarded as a coincidence, without any causative relation to the hernia.

Friedman states: "As an independent condition, that is, without a true hernial sac accompanying it, fat hernia is comparatively uncommon. There are more often present both fatty mass (extraperitoneal) and hernial sacs, with or without contents. But this is not true fat hernia, and should not be termed as such. A pure fat hernia is extraperitoneal in origin, and is not accompanied by peritoneal sac." Friedman further states: "Fat hernia may be found in the inguinal or femoral canals, at the linea alba, between the umbilicus and ensiform cartilage, very rarely below the umbilicus; at the latter situation the lipoma protrusion, also with or without peritoneal sac accompanying it. In the female it is more often present in the femoral than the inguinal region, while the reverse is the case in the male."

I would agree with Friedman in the latter statement, except that I would leave out the word "hernia" and substitute "lipoma," or fatty tumor. Such masses of fat are extremely common in femoral hernia in women, but I would not call them *herniae* unless accompanied by a peritoneal sac; nor do I believe they can be properly designated as "fat *herniae*" unless it can be demonstrated that the fatty tumor is an important etiological factor in the production of the hernia, which I do not concede.

With regard to diagnosis, it may be difficult to differentiate a mass of fat in the inguinal or femoral canal from an irreducible omental hernia, but the history of previous reducibility may be of great help. If there is no hernial sac present, the condition needs no surgical treatment. If the inguinal canal is opened, and a mass of fat is found which is shown not to be connected with the omentum, my experience has been that we are almost certainly dealing with a bladder hernia,

and the utmost caution must be exercised to prevent injury to the bladder wall.

TWO COMPARATIVELY RARE FORMS OF HERNIA (EXTERNAL SUPRAVESICAL HERNIA and INTERNAL VENTRAL HERNIA)" is the title of an extensive paper by Steimker.<sup>1</sup>

### I. *External supravesical hernia.*

Kocher and Quervain consider this type of hernia as extremely rare. Steimker states that this assumption, however, is only partly correct, that is, insofar as the retroperitoneal or internal type of hernia is concerned. External supravesical herniae are much more frequent than has been believed up to recently. Reich reported 26 such cases. The reason why these herniae have received so little notice by the writers of text-books, Steimker believes to be that, in the first place, they cannot be definitely distinguished from a direct inguinal hernia before operation, and secondly, their treatment is exactly the same as that of direct hernia.

Steimker gives brief histories of 8 cases collected, in addition to those reported by Reich, and describes very fully, the autopsy findings in a case of external supravesical hernia combined with lateral ventral hernia observed at the Anatomical Institute at Göttingen.

From a study of the published cases, Steimker states, it appears that herniae of the supravesical fossa are by no means always of the same formation, and, according to their origin, must be divided into three different classes, namely, internal, intermuscular, and external herniae. In the first, the hernial sac is situated retroperitoneally and shows no tendency to pass into the layers of the abdominal wall. In the second variety, the hernia has protruded into the abdominal wall itself, but has not yet perforated the same. Here distinction must be made between the true intermuscular herniae, which are prevented by the strong aponeurosis of the external oblique, from reaching the external inguinal ring, and hence, are doomed to remain interstitial, and such herniae as are still in process of development, pushing forward in a straight line to the external inguinal ring, without as yet having reached the latter.

This latter class belongs to the third variety: the external supravesical herniae. They either find their way through the aponeurosis of the external oblique medially to the external ring, and then remain as bubonoceles laterally to the root of the penis, or they emerge through the external ring and descend into the scrotum.

Entirely different are the conditions found in retroperitoneal hernia of the bladder. These bladder evasions, being situated extraperitoneally, cannot pass into the supravesical fossa. As they have no peritoneal sac, they are not herniae in the true sense of the word. The combined presence of an external supravesical hernia and one, or even more, other herniae is a fairly frequent phenomenon. Not less than

<sup>1</sup> *Beit. z. klin. Chir.*, 1913, Band lxxii, Heft 3.

18 of the 32 cases described occurred in conjunction with one or more herniae which speaks for a decided weakness of the entire region in question, in these individuals.

As in other forms of hernia of the inguinal region, the right side is more frequently affected than the left in these extrasupravesical herniae, the proportion according to Steinker being 19 to 9, on a basis of 28 cases in which the site was stated.

Of 27 cases in which the sex was given, only 3 were women.

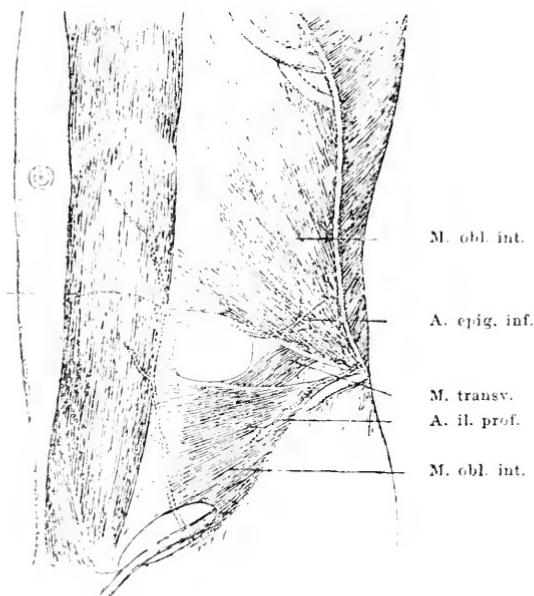


FIG. 28.—Lateral ventral hernia.

As regards the clinical symptoms, Steinker states that 65 per cent. of the cases of external supravesical hernia appear as a tumor with a pronounced inward diagonal course, or they appear in the neighborhood of the inguinal ring itself. The hernial opening is frequently characterized by extraordinary narrowness and hardness, which explains the high percentage of incarcerations (33 per cent.). Other fairly frequent complications are bladder disturbances, even though the bladder be not contained in the hernial sac.

The diagnosis can but rarely be made before operation, and often presents considerable difficulty even during operation, which is confirmed by the fact that the description of most of the cases, dated since 1804, is based on the autopsy findings.

Steinker refers to the publication of Sthümer, covering 41 cases in all, and appends 8 additional cases which he found in the literature.

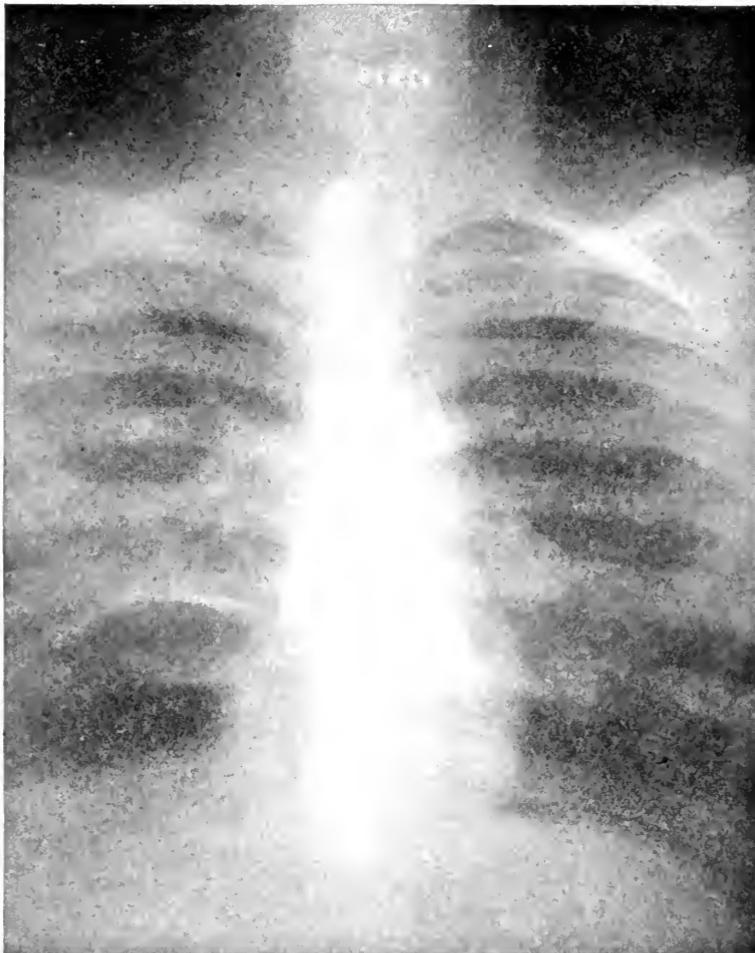


FIG. 29.—June 26, 1911. Case, diaphragmatic hernia, with the stereoscopic radiogram made of patient in the vertical position, the sternum next to the x-ray plate, care being taken to avoid any rotation of the spine on its long axis. The central focus corresponds to the level of the seventh dorsal vertebra. We are viewing the thorae through from behind, therefore the right side of the print represents the right side of the thorax. These prints are faesimile reproductions of the original plates. Note the position and outline of the pericardial shadow. The heart inclines strongly toward the right, its right border extending a greater distance to the right of the midsternal line than does the left border to the left of the spine. Both hiluses are abnormally dense, the left being markedly enlarged. Both apices are clear and the pulmonary tissue is normal in all three right lobes and in the upper left lobe. In the lower portion of the left thorax can be seen clearly a curved white line of greatly increased density. The proximal end of this line is opposite the level of the spinal juncture of the eighth rib on the left side. From this point the line curves outward along the eighth interspace to the ninth rib. Between this line and the upper border of the tenth rib is seen a dark area of greatly decreased density, through which one can clearly distinguish branches from the lower pole of the left hilus. The costal portions of three ribs are also visible. The left margin of the pericardial shadow is not clearly defined. Note the clear-cut outline of the dome of the diaphragm to the right of the spine and compare it with the faint, indistinct outline on the left of the spine, which is to be seen just below the tenth rib. The unusual appearance of the lower portion of the left thorax attracted our attention and suggested strongly the probability of a hernia of the diaphragm. A study of the stereoscopic plates supported this suspicion, and it was deemed important to establish the position of the stomach, for it seemed likely that the dark shadow below the abnormally placed curved line was due to gas in the stomach. With this end in view an emulsion of subcarbonate of bismuth and acacia was given the patient by mouth and a second set of plates made immediately, the patient being in the vertical position. (See Fig. 30.)



FIG. 30.—Radiographed immediately after the ingestion of bismuth subcarbonate emulsion. (Compare with Fig. 29.) Note the line of demarcation between the white dense area and the dark area lying above it. The white shadow represents bismuth in the stomach, the upper border of the shadow representing the surface level of the emulsion. Above the bismuth is seen the gas-bubble of the stomach. This is limited above by the wall of the stomach, which we recognize as the curved line described in Fig. 29. Note the faint outline of the bismuth lining the esophagus. This can be traced upward to the limit of the plate. Figs. 29 and 30, together with the history, confirmed the diagnosis of hernia of the diaphragm. Important diagnostic points demonstrated by the radiograms, Figs. 29 and 30: (1) The presence of a dark circumscribed shadow situated above the indistinct outline of diaphragm on the left side and bounded above by a curved dense band which does not maintain the dome shape typical of the normal diaphragmatic line, and limited mesially by the left border of the heart, which is displaced strongly to the right; (2) the presence of the shadows of the lower branches of the left hilus showing through rarefied area; (3) the location of the stomach and its great bubble by bismuth ingestion method.

Steimker states that it is often difficult to differentiate between the congenital and acquired type of lateral ventral hernia, inasmuch as it is characteristic of this form of hernia that the sac is empty, and even

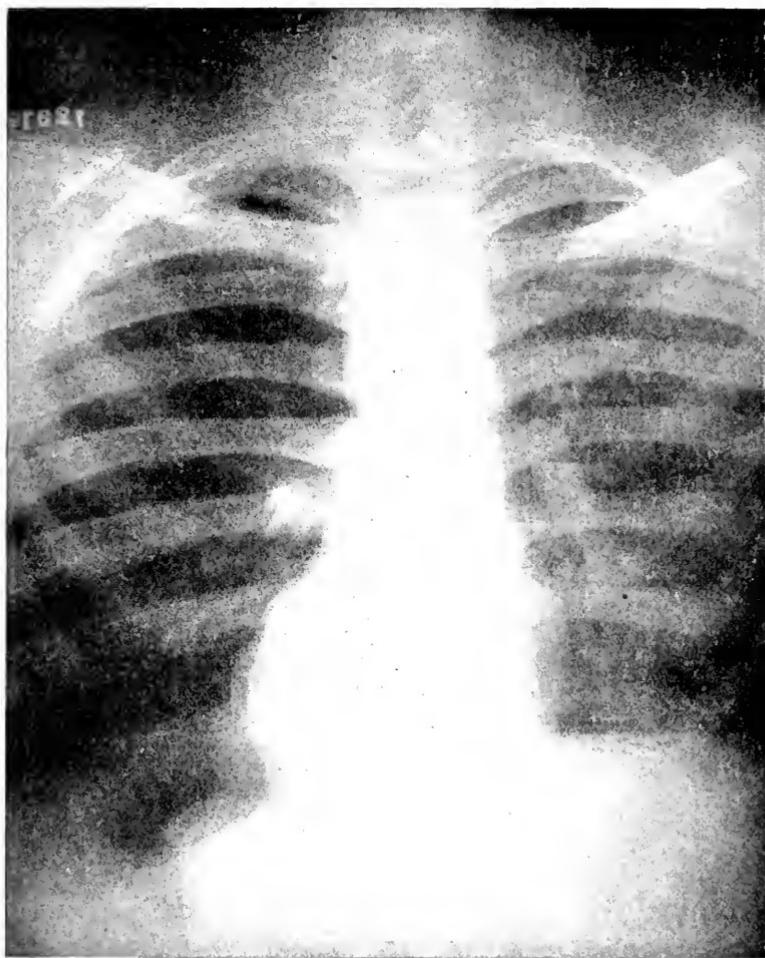


FIG. 31.—Two weeks after operation. (Compare with Fig. 29.) Patient's pose is the same as in Fig. 29. (1) Note the absence of the curved white line described in Fig. 29. (2) the dense white area just to the left and below the nose of the heart represents the operation scar; (3) the heart has returned almost to its normal position; (4) there is a marked difference in density in the two sides of the chest; the left is darker, indicating a pneumothorax and partial collapse of the pulmonary tissue incident to the operation upon the diaphragm.

such with contents, may exist for years without giving the bearer much trouble and come to notice only when incarceration occurs. Pronounced ascites and frequent pregnancies are predisposing factors.

As regards the ages, Steinker states that these herniae occur in the proportion of: 3 in children, to 10 up to the age of forty, to 27 in the later stage of life; the average being forty-three years. They are found as frequently on the left as on the right side. They occur with greater frequency in the female than in the male, in the latter in 59.5 per cent. of all the cases. The contents of the sac is usually gut, rarely omentum. The hernial opening is circular, or oval.

With regard to the diagnosis, Steinker states that the larger herniae can easily be recognized by the cushion-like swelling and the tympanitic sound. The smaller size hernia, particularly when situated intermuscularly, has few pronounced clinical symptoms; in cases of incarceration there is great resemblance to appendicitis with abscess formation, which increases the difficulty of rendering a correct diagnosis. Nevertheless, the latter is possible so long as one takes into consideration the possibility of the existence of such a hernia.

**DIAPHRAGMATIC HERNIA.** An important paper on the *Diagnosis of Diaphragmatic Hernia* has been published by H. Z. Giffin,<sup>1</sup> of Rochester, Minn. Giffin states that 650 cases have been reported, *i. e.*, 500 cases prior to 1901, 107 since then, in addition to which he himself has collected 41 cases. The great majority of these were either congenital herniae in infants, or herniae that produced few or no symptoms during life and were discovered only at autopsy. In only 15 cases was the diagnosis probably correctly made during life.

Of 4 cases of diaphragmatic hernia operated upon at St. Mary's Hospital (Mayo Clinic), three were reported by Beckman in 1909, the fourth case by Giffin.<sup>2</sup> In the latter case, the diagnosis was made before operation; the history of severe injury a year before, rendering the diagnosis less difficult. The patient, a man, aged twenty-six years, had been caught together with four other men, two of whom were killed, in a sand slide; he was instantly and forcibly doubled up with his head between his feet, was unconscious for five or ten minutes. The stomach was empty at the time of the accident. Half an hour later the patient experienced severe pain over the entire abdomen and chest, and shortness of breath. The symptoms continued for two weeks. The diagnosis was made without the aid of the *x-ray* examination, and was confirmed by bismuth test. For a full history the reader is referred to the report.

Upon reviewing the case, Giffin states, "It appears that a history of severe trauma, followed by upper abdominal and left thoracic pains, dyspnea, and vomiting, together with physical findings pointing to displacement of the stomach or intestine into the lower left chest and of the heart to the right, will ordinarily be sufficient for making a diagnosis of diaphragmatic hernia. If the history and findings be definite, this will be true whether the patient is seen immediately after injury

<sup>1</sup> Annals of Surgery, March, 1912.

<sup>2</sup> Loe cit.

or some time later. Roentgen-ray findings will then be mostly of corroborative value. When, however, the injury has been less severe, and the symptoms and signs less definite, and, again, in most cases of congenital diaphragmatic hernia, radiographic and fluoroscopic examinations must be relied upon for a differentiation of the condition. In interpreting the plates, (1) a destruction of the definite dome shape, characteristic of the normal diaphragm line, (2) the appearance of lung tissue through the gas-bubble in the left chest, and (3) the demonstration of bismuth in the colon above the level of the bow line of the chest, constitute the most important evidence in favor of hernia of the diaphragm. By fluoroscopic examination, the "paradoxical respiratory phenomenon" may be demonstrated."



FIG. 32.—*x-ray photograph after bismuth meal.*

The writer appends a short bibliography, but a fuller one, containing 187 references, can be had on application to Dr. Giffin.

Waelli<sup>1</sup> reports a case of *congenital diaphragmatic hernia* in the foramen Morgagni, successfully operated upon by Quervain, at the Bâle Clinic. Waelli states that this case belongs to the rare exceptions in which the diagnosis of a congenital anomaly of the gut with possible involvement of the diaphragm, is made before operation, or even before death. Struppner collected 13 cases in which the diagnosis of diaphragmatic hernia was made. According to Lacher, in a series of 270 cases, the probable diagnosis of diaphragmatic hernia was made in but 7 cases.

<sup>1</sup> Arch. f. Clin. Chir., 1912, Band xevii, Heft 4.

In the case reported by Waelli, the *x-ray* photograph, taken after a bismuth meal, revealed the condition shown in the accompanying



FIG. 33.—*x-ray* photograph after bismuth *per rectum*



FIG. 34.—*x-ray* photograph after bismuth meal given after operation.

illustration (Fig. 32). Another *x-ray* taken after a larger injection of bismuth *per rectum* (Fig. 33) demonstrated the presence of a stenosis in the region of the kink in the transverse colon.

Waelli states that Lacher's tabulated statistics contain but 9 cases in which the hernia positively entered from behind the sternum. The accompanying Fig. 34, taken subsequent to the operation after a bismuth meal, shows the colon to have resumed its normal position, the difference in caliber to have been equalized, and the function restored.

On the basis of his investigations, Waelli believes that the *x-ray*, in conjunction with physical and clinical examinations, enables us, in a certain number of cases, to render the diagnosis of diaphragmatic hernia, and he further believes that it is possible by means of the *x-ray*:

1. To differentiate between a hernia and an eventration. In the latter there is always a linear shadow over the organs in the anterior portion of the thorax. This shadow pulsates with respiration without changing its contour.
2. To determine the contents of the sac.
3. To ascertain the location of the hernial opening, as well as of those parts of the gut not contained in the sac.
4. The question as to whether the hernia be a true hernia or a false one, cannot be decided beforehand, nor can it be determined whether a hernia be of the congenital or of the acquired type.
5. The fact that the *x-rays* plus bismuth meal enable us to observe the results of the operation, certainly is of value.

# SURGERY OF THE ABDOMEN, EXCLUSIVE OF HERNIA.

BY JOHN C. A. GERSTER, M.D.

The Present Status of the Röntgen-ray Examination of the Gastro-intestinal Tract is well summarized in two papers, one by Carman<sup>1</sup> in English, the other by Holzknecht<sup>2</sup> in German. The accepted facts are given in a terse, clear fashion; most of these have already been brought to the reader's attention in the June numbers of PROGRESSIVE MEDICINE for 1912 and 1913. Conditions about which doubt still exists will be reviewed at suitable points in the various sections which follow.

Leaders in Röntgenology all emphasize the absolute necessity for repeated critical examinations a number of days or weeks apart, to avoid mistaking transient functional disorders for permanent pathological lesions. Moreover, practically every paper states that a correct interpretation of the *x*-ray plates cannot be made without also taking into consideration all the clinical facts. These warnings are not new; but their repetition is justified, considering some rather doubtful assertions made during the past year which have furnished excuses for performing various plasties upon the intestines.

In diagnosing the alimentary ailments of children, the *x*-ray has proved of great value.<sup>3</sup> This is especially true of congenital pyloric stenosis<sup>4</sup> and of Hirschsprung's disease. On the other hand, lesions outside of the digestive tract, such as kidney or bladder stone,<sup>5</sup> giving symptoms chiefly referable to the stomach and intestines, have had their true character revealed by the *x*-rays, thereby saving much time in reaching a correct diagnosis.

**Experimental Abdominal Surgery** has received valuable additions to its facilities in the "visceral organism" of Carrel<sup>6</sup> and the "spinal cat" used in many physiological laboratories. The technique of preparing the visceral organism is relatively simple. The trachea and esophagus

<sup>1</sup> Journal of the American Medical Association, vol. lxi, p. 321.

<sup>2</sup> Wiener med. Woch., 1913, No. 32 and 33, pp. 1965 and 2038.

<sup>3</sup> Chapin, Journal of the American Medical Association, vol. lxi, p. 1419.

<sup>4</sup> Scudder, Annals of Surgery, February, 1914, p. 239, and Mixter, Boston Medical and Surgical Journal, 1913, No. 9, p. 309.

<sup>5</sup> Morse, Journal of the American Medical Association, vol. lxi, p. 1422.

<sup>6</sup> Journal of Experimental Medicine, 1913, No. 2, p. 155; also Bull. méd. 1913, vol. xxvii, p. 27.

of an anesthetized animal are exposed and isolated in the neck; they are cut across; a stomach-tube is tied into the esophagus and the trachea is connected with an artificial respiration apparatus. Dissecting extraperitoneally, the iliacs are tied, and the pelvic and abdominal viscera are loosened in one mass. (The gut is ligated and cut at any convenient point.) Artificial respiration is started as the thorax is opened; the subclavians and carotids are tied; with the latter act, the animal, as such, is virtually killed. For a few moments the heart slows markedly (vagus stimulation) and then picks up its former rhythm. The aorta and cavae are freed posteriorly by systemic ligation of the intercostals and division of the diaphragm. The organism is now free, and can be transferred to a suitable receptacle containing a quantity of Ringer's solution at body temperature. The easiest way to keep up the required degree of warmth is to place the organism with its container in an incubator. During the operation, the exposed viscera should be covered with greased handkerchiefs to prevent drying.

The spinal cat's preparation is still simpler. After establishing a connection between the trachea and an artificial respiratory apparatus, the carotids are ligated and what amounts to decapitation is then performed. The shock of this passes off rapidly, and the heart resumes its normal rhythm.

These collections of living viscera have lived as long as thirteen hours. They apparently die from lack of water. Probably they can be kept going much longer if supplied with fluid in a suitable manner. It is easy to see how readily they lend themselves to the study of acute abdominal conditions; for example, the different forms of obstruction.

Katsch and Borchers<sup>1</sup> sewed a window of thin celluloid into the abdominal wall through which they have been able to observe movements of the intestine following the administration of food, drugs, and the application of direct stimuli such as changes in temperature or electricity. Their experiments were carried out upon rabbits.

The most important book upon abdominal surgery which has appeared during the past year is Volume III of the *Handbuch der praktischen Chirurgie* (4th ed.), edited by Bruns, Garré, and Küttner. It is a pity that the conditions of medical life in this country do not afford sufficient leisure for the production of many similar original works in our own language. To enumerate the various points of special interest would take too much space without conveying any definite facts of practical value to the reader.

**Crile's Anoxic-association Anesthesia in Abdominal Surgery.** This distinguished author recently has published<sup>2</sup> a series of 4401 laparotomies (unselected cases), with a mortality of 1.6 per cent. Briefly, the method consists in preventing either psychic or traumatic impulses from reaching

<sup>1</sup> Zeitsch. f. Exper. Path. u. Therap., 1913, pp. 225 to 294.

<sup>2</sup> American Journal of Obstetrics, 1913, vol. lxviii, p. 309.

the central nervous system. One hour before operation, the patient receives an injection of scopolamin and morphin. The nitrous oxide-oxygen narcosis is started with the patient in bed in his own room. The operation proper is performed under both general and local anesthesia. Crile believes that under the customary general narcosis, although the patient is not aware of them, sensory impulses reach and damage the central nervous system just as much as though no anesthetic had been used. For this reason, local anesthesia is used upon the unconscious patient to block harmful impulses to the central nervous system. Crile prefers novocain for the abdominal wall, and quinine-urea-hydrochloride for the peritoneum, both parietal and visceral, because this latter anesthetic lasts after the operation, and therefore lessens the postoperative pain and shock.

In clinics where time is no object, this method should be the routine one; but when much work must be done within a given time, the method will necessarily be reserved for urgent operations upon those enfeebled by age, disease, or trauma.

**Transverse Abdominal Incisions** continue in favor on the continent. Verhoogen,<sup>1</sup> who employs transverse incisions almost exclusively, points out that inadequate reunion of the divided recti, especially in wounds below the umbilicus, is very apt to be followed by herniae which are most difficult of repair. If, on the other hand, the peritoneum and especially the external aponeurosis are united with care and exactness, there need be no fear of hernia, provided, of course, there is no infection. Drüner<sup>2</sup> has called attention to the fact that a relatively small incision parallel with the outer margin of the rectus and near the costal margin, will divide most of the motor nerves supplying the rectus muscle. While not new, this is a fact which cannot be too frequently emphasized.

**The Rupture of Abdominal Wounds** is a subject of never failing interest. The location of the wound has very little to do with the probability of its spontaneous reopening. In some instances, the peritoneum is the only layer remaining intact, while in others, all the layers part, allowing the escape of viscera. Badly nourished subjects seem peculiarly prone to this accident. Examination of the reopened wound reveals an entire absence of any connective-tissue production. There is no infection; the muscle, fascia, and fat look as though the wound had been made the day before, instead of the two weeks that usually have intervened. Recently Halpern,<sup>3</sup> a Russian surgeon, has published a series of 25 such cases, 5 of which are from his own practice. According to his analysis, it made no difference whether the suture material was absorbable or

<sup>1</sup> Ann. de la Soc. Belge de Chirug., 1913, vol. xxi, p. 12.

<sup>2</sup> Zentralbl. f. Chir., 1913, No. 30, p. 1183.

<sup>3</sup> Weljaminow's Surgical Archives, vol. xxviii, p. 918. (Russ) cit. after Zentralbl. f. Chir., 1913, p. 975, and Zentralbl. f. die gesamte Chir. u. i. Grenzgeb., Bd. i, p. 263.

non-absorbable, or whether one, two, or three layers of sutures were made. Causation was furnished by any sudden contraction of the abdominal muscles, such as sneezing, coughing, or vomiting. I know of one man whose abdominal wound ruptured when he petulantly threw himself to one side of the bed in the course of an altercation with his wife who was not using the tact desirable while visiting the sick room. As a rule, the results of this accident are not serious; the wound is closed again and heals. If one fears infection, a strip of rubber dam can be led out of the lower angle.

**The Control of Oozing within the Abdomen.** A large amount of experimental work has recently been done in this field. Many kinds of tissue have been tried with more or less success. The control of oozing from the liver after extirpation of the gall-bladder has occupied the main attention of the different authors. However, the various methods apply just as well to the control of oozing from other parenchymatous organs or from surfaces denuded of their peritoneal investment.

*Fat*, obtained from beneath the margins of the abdominal wound, has been advocated by Hilse<sup>1</sup> for this purpose. His experiments were carried out upon rabbits; to these are added two clinical experiences.

*Pieces of muscle* applied to the oozing liver surface are recommended by Laewen, and Opokin and Schamoff.<sup>2</sup> The latter worked upon dogs. Three months after implantation, the flaps showed almost complete disappearance of muscular tissue with an extensive production of connective tissue. Investigation was also made to determine which tissue contains the greatest amounts of thrombokinetic substance. It was found that extract of lung tissue was the most powerful in causing coagulation (see below); next to lung, came muscle. Regarding the latter, it may be of interest to remark that some time ago Harvey Cushing called attention to the value of bits of muscle (obtained from the temporalis) applied to the brain in checking oozing.

*Fascia* has been used by Henschen, Kirschner, Chessin, Ritter, and J. S. Davis. It healed firmly, and apparently is a more suitable tissue than muscle or fat. It has been taken from the anterior sheath of the rectus or from the fascia lata.

*Flaps of peritoneum* have been dissected free and have been applied to the oozing surfaces by Clairmont and Negri. Like all the preceding transplants, they, too, became converted into a mass of dense connective tissue.

*Both free and pedunculated flaps of omentum* have been successfully used upon animals and patients. Loewi, Boljarsky, and Girkolaff have made investigations in this field. More recently Jacquin,<sup>3</sup> working upon dogs, has recommended the use of free flaps of omentum because

<sup>1</sup> Zentralbl. f. Chir., 1913, No. 48, p. 1849.

<sup>2</sup> Original in Russian, cit. after Zentralbl. f. d. gesamte Chir., Bd. ii, p. 145.

<sup>3</sup> Archiv. f. klin. Chir., Band cii, Heft 2, p. 502.

they can be more accurately applied to the raw oozing surfaces. That is, the flap just covers the denuded surface; an accurate marginal suture holds it in place. Oozing from the spleen was as readily controlled, by this method, as oozing from the liver.

At the end of two months, the omental flap was found to consist almost entirely of connective tissue.

From the foregoing we see that in many instances the transplanted tissue heals in place, its intrinsic cells die, there is a round-cell infiltration, and eventually connective tissue replaces the original transplant. Dense adhesions generally surround such transplants; it is always a matter of chance whether these will or will not cause trouble.

Of course, the use of pedunculated omental flaps is as old as abdominal surgery itself.

Stuckey<sup>1</sup> has reported the case of a woman who died of heart failure seventy-two hours after cholecystectomy. At the operation, control of bleeding by hemostats was ineffectual. A piece of omentum was cut off and was firmly applied to the oozing surface for two minutes. It was then seen that the bleeding had stopped and that the transplant adhered of itself in place. At autopsy, three days later, the piece of omentum was found firmly adherent to the liver. There was no collection of blood beneath it, and there was no adhesion to its free aspect (whether this would have continued to remain free, could not be determined).

*The most powerful coagulating agent known at present*, is an extract of lung tissue called "thrombokinase" by Strong,<sup>2</sup> its discoverer. A similar agent has been extracted from mammalian blood plates by Fonio,<sup>3</sup> an assistant of Kocher's; its official name is "Coagulin, Kocher-Fonio." Both of these agents have proved most efficient in causing a prompt clotting. Care must be taken to bring the coagulating agent directly in contact with the open lumen of the bleeding vessel. At present, these extracts are expensive, and are not supposed to keep well.

**Drainage of the Peritoneal Cavity.** The more advanced surgeons of today are inclined to limit the use of gauze to purposes of hemostasis. For a number of years the Mayos have been opposing the leading of gauze drains down to suture lines closing hollow viscera; they have maintained that if one really desires to obtain a leak, the surest way is to pull out some gauze which has been lying in contact with a suture line for a few days. Instead, they use rubber dam or rubber tissue. Other men use very soft rubber tubes which amounts to the same thing. The recent experiments of Petroff<sup>4</sup> upon rabbits bear this out. Petroff found that from aseptic abdominal cavities, after five to six hours,

<sup>1</sup> Original in Russian, cit. after Zentralbl. f. d. gesamte Chir., Band ii, p. 322.

<sup>2</sup> New York Medical Journal, March 23, 1912.

<sup>3</sup> Korrespondenzblatt f. Schweizer Aerzte, 1913, Nos. 13 and 15.

<sup>4</sup> Original in Russian, cit. after Zentralbl. f. d. gesamte Chir., Band ii, Heft 5, p. 261.

the gauze drains showed a much diminished capillarity, and that by the end of fifteen to twenty-four hours, drainage from the free peritoneal cavity has ceased altogether. The process depended upon the formation of adhesions and the gradual loss of the hygroscopic power of the gauze. In the presence of peritonitis, the isolation of gauze strips by adhesion formation was less marked; the hygroscopic qualities were lost just as quickly. The escape of secretions occurred alongside the gauze, not through its meshes. In the depths, the gauze wicks lay as slime-covered foreign bodies between the viscera. Regarding fenestrated rubber tubes, it was found that the openings were frequently blocked by loops of intestine; drainage was still present at the end of fifteen hours. With glass tubes, complete isolation by adhesions did not take place even after forty-eight hours had passed. The introduction of gauze strips within the drainage tubes, and their frequent change, was found to be a distinct aid to effective drainage.

Deaver, in discussing Coffey's paper on adhesions (see below), emphasizes the point that if gauze has been used, it should not be pulled loose. He says,<sup>1</sup> "I tell my house doctors to leave it in until it practically comes out of itself."

Every year new or rediscovered METHODS OF DRAINAGE IN CHRONIC ASCITES appear, are tried with apparent success, and drop out of sight. So far, no method has given sufficiently uniform satisfaction to justify its adoption as a standard. This year Henschen<sup>2</sup> has suggested the use of a soft collapsible tube of thin rubber (finger cot with the blind end cut off), for establishing drainage between the peritoneal cavity and the subcutaneous cellular tissue. Evler<sup>3</sup> makes a gap in the rectus, large enough to admit a finger; this is lined with peritoneum sutured to the fascia. It was employed in 3 cases of tuberculous peritonitis. Henschen used, without success, the sac of a femoral hernia for the same purpose in carcinomatous ascites.

**Adhesions.** This subject has been brought up to date in a forceful article by Coffey.<sup>4</sup> He says:

"I have had the literature on this subject completely abstracted at the Surgeon-General's Office. The most striking features of the literature are its monotony and its inconsistency. All authors have discussed prevention, *e. g.*, all authors have discussed the wet and dry protective pads, one maintaining that he had performed 132 laparotomies with dry asepsis, with 10 deaths, 5 of which were due to intestinal obstruction, while in 76 cases treated with moist asepsis, he had two deaths and no intestinal obstruction.

An equally prominent authority reported 481 laparotomies with dry asepsis, and only one fatality from ileus, while with moist asepsis

<sup>1</sup> Journal of the American Medical Association, vol. lxi, No. 22, p. 1957.

<sup>2</sup> Zentralbl. f. Chir., 1913, p. 41.      <sup>3</sup> Med. Klin., 1913, Band ix, p. 214.

<sup>4</sup> Journal of the American Medical Association, vol. lxi, p. 1952.

he had a much higher rate. Other operators assert that exposure to the air is the principal cause of adhesions. Others that trauma is the principal cause, and still others that sepsis is the chief cause. Every variety of lubricant that has ever been known has been used by ardent advocates to prevent adhesions, and condemned even more ardently by others who have tried them. Some have used prepared membranes

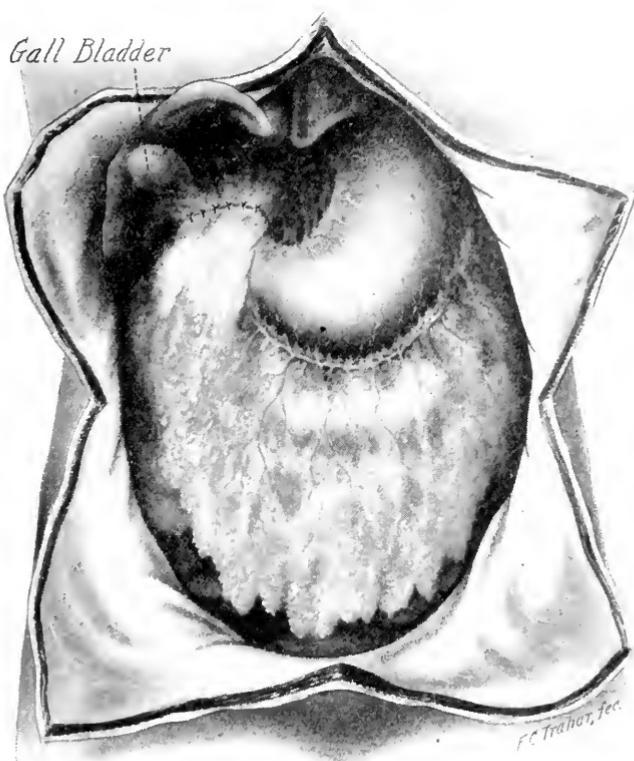


FIG. 35.—Reflected free edge of greater omentum sutured to lesser omentum for the purpose of separating the gall-bladder from the duodenum, thus preventing the reformation of adhesions. (Coffey.)

with good results, while others equally prominent got no results. Some have no adhesions by using cathartics; others get equally good results by absolute rest treatment. By carefully considering all the literature along with my own limited personal observations, the following negative deductions may safely be reached:

1. The choice between the wet and dry pad is not vital, if equal care is used in their use.

2. Oils and all lubricants are worse than useless in the prevention of adhesions.<sup>1</sup>
3. Specially prepared membranes and other foreign bodies have not proved equal to the claims of their advocates.
4. Cathartics following operation probably do more harm than good, as a rule, although at times they may be of benefit.

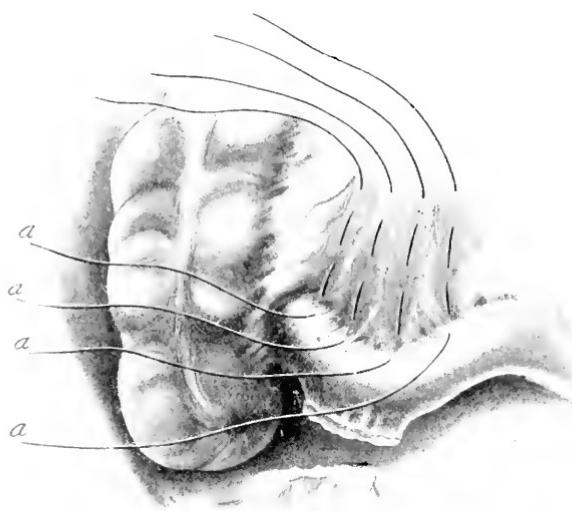


FIG. 36.—Method of applying purse-string sutures for the purpose of shortening the mesentery of the ileum to prevent reformation of Lane's bands. *a*, purse-string sutures. (Coffey.)

On the other hand, we are safe in the following positive deductions:

1. Thorough asepsis.
2. As little handling as possible.
3. Avoidance of all traumatism and exposure to the air, as far as can be.

All of these agencies and precautions undoubtedly have an influence, but of greater importance is the special resisting power of the patient. Adhesions forming under given circumstances probably are in exact ratio to the patient's power of resistance to sepsis. Adhesions ordinarily do no harm as far as the patient knows. Adhesions do harm only when they impair the motility of a normally movable organ, and pre-

<sup>1</sup> See Camphor Oil in Peritonitis, and review of Pope's work on adhesions below.

vent it from performing its normal function. Adhesions which tend to disturb the normal relation between a freely movable and a relatively fixed portion of the gastro-intestinal tract often produce a partial obstruction at these points."

There is nothing very new in Coffey's recommendations: (1) To cover denuded surfaces by uniting the adjacent peritoneum over them; or (2) when this is not feasible, to use omentum or mesentery for the same purpose (Fig. 35); (3) if the foregoing is not convenient, to anchor, the adherent organ away from its point of attachment (Fig. 36). When a loop of intestine is found to enter a mass of adhesions in an inaccessible locality and symptoms of obstruction have been present, Coffey makes a side-to-side anastomosis. This is far more likely to relieve the obstruction than to liberate all the adhesions only to have them promptly reform.

For the past six years, Coffey has protected his gauze drains with rubber tissue. In a number of his drained cases reopened for some other cause he was impressed by the absence of adhesions. This coincides with the facts brought out in the section on "Drainage" (see above).

Saxton Pope,<sup>1</sup> in his most instructive article on the production of adhesions, makes the statement that among the series of exudates produced by the introduction of various substances into the peritoneal cavities of rabbits, none presented a worse appearance than the experiment with camphorated oil. (See Camphor Oil in Peritonitis below.) Here there was a thick, creamy deposit, masses of fibrous lymph, large plaques of camphor adherent to the mural peritoneum and under the diaphragm, and dense, resistant adhesions throughout the entire abdomen. The appended table gives Pope's results.

|  | Exudate. | Adhesions. |
|--|----------|------------|
| Control                                | +        | ++         |
| Tincture iodine                        | ++       | ++         |
| Camphorated oil                        | +++      | +++        |
| Olive oil                              | ++       | ++         |
| Petrolatum                             | ++       | ++         |
| Butter                                 | ++       | ++         |
| Sugar, 50 per cent. solution           | +        | ++         |
| Citrated sugar                         | +        | +          |
| Egg albumen                            | +        | +          |
| Citrated egg albumen                   | ++       | +          |
| Milk                                   | +        | +          |
| Peptonized milk                        | +        | -          |
| Ringer's solution                      | -        | ++         |
| Salt solution, normal                  | -        | +          |
| Ammonium oxalate, 1 per cent.}         | -        | +          |
| Salt solution                          | -        | -          |
| Citrate of soda, 1 per cent.}          | -        | -          |
| Salt solution                          | -        | -          |
| Sodium citrate, 2 per cent.}           | -        | --         |
| Sodium chloride, 4 per cent.}          | -        | --         |
| Citrate of soda solution, 2 per cent.} | -        | --         |
| Salt solution, 3 per cent.             | -        | --         |

<sup>1</sup> Annals of Surgery, January, 1914, p. 101.

As one can see, citrate of soda in salt solution gave the best results. Pope says, "after an impartial scarification, which under normal circumstances at the end of a week would give a nasty peritoneum, with the addition of citrate solution we have an abdomen practically free from exudate, no adhesions; sometimes the endothelium shows no sign of insult other than an opacity and thickening." According to Pope, the best medium consists of citrate of soda, 2 per cent., with hypertonic salt solution, 3 per cent. He concedes that "probably the best medium for carrying the citrate solution has not been found."

He does not assume that citrate solution will prevent adhesions where large denuded areas of the peritoneum are exposed. Naturally, such areas should be covered by suitable plastics. *Addendum.* Intravenous injection of comparatively large amounts of citrates and oxalates in rabbits failed to elicit any toxic effects.

Contrary to the usual extravagant assertions one is accustomed to see in most of the "arbeits" upon the prevention of peritoneal adhesions, Pope modestly states that these laboratory results are applicable only as a mild preventive measure during such abdominal operations which ordinarily tend to leave more or less agglutination and troublesome postoperative adhesions.

It is not suggested that large quantities of solution be left in the abdominal cavity, although in the absence of pus it is not detrimental to do so, but that 1 or 2 per cent. of citrate of soda be added to the usual operating-room solutions of normal saline. This has actually been done by Terry in his abdominal work at the hospital of the University of California.

**CAMPIOR OIL IN PERITONITIS.** Last year several unfavorable reports were cited. This year, Momburg<sup>1</sup> contributes some significant observations which seem to confirm those views. Within a short time (autopsy finding twelve hours, postoperative) the oil collects in the pouch of Douglas, where it remains for days (see below), evoking local peritonitis which certainly does not hasten convalescence. Blecher<sup>2</sup> had 5 cases of diffuse peritonitis, in every one of which an abscess formed in the pouch of Douglas. It was noted that when an appreciable amount of exudate was present, the oil formed a thin layer upon its upper surface. Blecher, by some curious reasoning, holds this abscess formation to be a good thing. Momburg, on the other hand, points out that in feeble patients this additional strain is often just sufficient to turn the tide against them.

Oil does not prevent the formation of adhesions. In a case of peritonitis, reopening showed extensive adhesions.

Oil as a vehicle for local anesthesia was tried in one case. A man, aged fifty-seven years, with marked cachexia from a pyloric carcinoma,

<sup>1</sup> Deutsch. med. Woch., 1913, No. 12, p. 556.

<sup>2</sup> Münch. med. Woch., 1913, p. 1261.

had 0.5 per cent. novocain in olive oil injected into the free peritoneal cavity twenty minutes before operation; in addition to this, he received a hypodermic injection of morphin. The operation was not entirely free from pain; however, a general narcosis was not necessary. He died at the end of eight days. Autopsy showed an intact suture line, distended intestines, oil drops in the pelvis, with an intense inflammatory reaction. Momburg ascribes this death to the use of oil.

Whether the employment of mineral oil instead of olive oil makes a very important difference, has not been determined.

**Lavage of the Inflamed Peritoneal Cavity with Ether** has been enthusiastically advocated by certain French surgeons for the past two years. It has been transplanted to Chicago by De Tarnowsky,<sup>1</sup> who reports a series of 30 cases in which results were good. The ether is supposed to be harmless to the serosa and harmful to the infecting bacteria. We know of no such selective action. If ether does not harm the peritoneum it does not damage the bacteria. Other reports<sup>2</sup> are not convincing.

**The Advantages of Plain Water for Proctoclysis** rather than normal saline solution, were briefly mentioned last year in connection with the preliminary announcement of Trout. In a later report, Trout<sup>3</sup> cites 2000 cases, in half of which saline was given; in the other, tap water. Instead of the hard rubber nozzle described by Murphy, a soft rubber catheter was used, and in the vast majority of cases the presence of this soft rubber catheter was not even known to the patient. The flow was regulated by means of the visible dropper described by Lawson.<sup>4</sup>

Trout made inquiry among most of the larger hospitals in this country as to their method of preparing normal saline solution. Replies, received from two hundred and thirty-two hospitals, showed that there was no uniformity in preparation of the saline solution, and that in most hospitals the solution was not isotonic with the blood. In passing, it was pointed out that replies from a number of hospitals indicated the employment of the same strength solution intravenously as well as per rectum. The danger of employing such solutions intravenously is apparent.

Taking as an average the directions for preparation given by the majority of the hospitals, plus the average amount of fluid absorbed through the rectum as stated in their reports, it was calculated that within the space of twenty-four hours, the average patient received as much salt as would be consumed as a condiment by a normal man in one month. The possible ill-effects from the absorption of this

<sup>1</sup> Journal of the American Medical Association, vol. lxii, p. 280. This article contains most of the references on the subject.

<sup>2</sup> Dergane, Wiener klin. Woch., August 14, 1913.

<sup>3</sup> Surgery, Gynecology and Obstetrics, May, 1913, p. 550.

<sup>4</sup> Journal of the American Medical Association, April 18, 1908.

quantity of salt upon the kidneys is pointed out by Trout in the following words:

"Even we surgeons know of the wonderful improvement in some patients with nephritis when placed on a salt-free diet, and all of us realize there is transient renal irritation or possibly nephritis following the majority of cases of anesthesia or infection. In 7 cases of our series, the following coincidence has been observed: A transient albuminuria remained in every specimen for two days after an anesthetic when using salt solution by rectum. Water was then substituted, and at the end of twenty-four hours the albumin had disappeared. At this time a return was made to salt solution, with reappearance of albumin and hyalin casts in from six to twenty-four hours. Patients were then placed on a limited salt diet, and the urine in every case promptly returned to normal and remained so until discharged from the hospital. In none of these cases was there any edema."

As said last year, water per rectum was well tolerated. Moreover, in cases in which water was administered, one-third more fluid was absorbed by rectum than in those in which saline was given, whereas in the latter nearly twice as much water was required by mouth to relieve thirst.

Trout says there is no more reason for the use of salt solution by rectum to prevent and relieve thirst than by mouth under like conditions. He believes surgeons have simply drifted into employing saline solution by rectum without giving the method sufficient consideration—and he is right.

**Hormonal.** In this section, both last year and the year before, it was reported that in many instances injections of hormonal were followed by collapse accompanied by chills and fever. Since then, Zuelzer, its discoverer, has asserted that these untoward effects were due to the presence of albumose in the original preparation and that the hormonal now on the market was free from albumose, hence had been purged of its former deleterious qualities. Others have experimentally and clinically tested the improved product. I shall cite a few of their more important findings, after which I believe my readers will agree that, as regards safety of this substance, there is still room for improvement.

At the Physiological Institute of the University of Leipzig, Dittler and Mohr<sup>1</sup> conducted experiments with hormonal upon rabbits under superficial ether narcosis; these showed that the new hormonal still contains albumose and vasodilatin. The degree to which blood pressure was lowered, varied in individual animals of the same species; it was transitory, and, while it continued, influenced the respiration and heart action.

<sup>1</sup> Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1913, Band xxv, p. 902.

Regarding the production of peristalsis, observations were made upon intestines flooded with warm Ringer's solution. In rabbits, two-thirds of the experiments were positive when up to 3 c.c. per kilogram of hormonal were used. On the other hand, dogs and cats reacted poorly. The large intestine was rarely affected. It was noted that the intestine floating in the Ringer's solution showed an active spontaneous peristalsis in animals not injected with hormonal. Slow injection, as advised by Zuelzer, even in high doses, failed to evoke peristalsis, although rapid injection was followed by peristalsis. Moreover, it was found that after injections of chloral hydrate (0.5 c.c. per kilogram), with which Zuelzer narcotized his animals, active peristaltic movements occurred which could be attributed to the fall in blood-pressure caused by the chloral.

Sehlagintweit,<sup>1</sup> of the Pharmacological Institute of the University of Munich, also tested the new hormonal said to be free from albumose.

In his first series of experiments, he used rabbits and cats; he did not open the abdomen. There was an invariable sinking in blood-pressure not increased by further slow injection. In rabbits, adrenalin prevented this lowering of pressure. The injection of creosote, which the hormonal contains, also caused a moderate fall in blood-pressure. There was no influence on the number or consistence of the bowel movements.

In a second series with the abdomen open, the effects of intravenous injections of hormonal were observed upon the intestines. Dogs and cats showed no reaction. In rabbits, active peristalsis occurred, not influenced by adrenalin or atropin.

In no instance was there evacuation of the large intestine. As in the first series of experiments, creosote alone also caused peristalsis. Experiments with guinea-pigs showed nothing which might be used to support the theory advanced that hormonal influences the internal secretion of the chromaffin system.

Sarnizin<sup>2</sup> reports intravenous and intramuscular injections upon twenty-one patients. Intravenous injection was invariably followed by a stormy general reaction of short duration. Intramuscular injections caused no reaction except a rise in temperature in 2 cases. A permanent result was obtained in 5 cases. Sarnizin advises the use of hormonal when other cathartics have failed, provided one bears in mind the proper contra-indications (whatever these may be). Schrieker<sup>3</sup> also reports clinical experiences with the intravenous injection of hormonal. Collapse, with rapid pulse, was accompanied by chills and fever, albeit the passage of flatus and stool followed within a short time.

<sup>1</sup> Archiv. Internat. Pharmacodynam., 1913, vol. xxiii, Nos. 1 and 2, p. 77.

<sup>2</sup> Original in Russian, cit. after Zent. f. d. ges. Chir. u. i. Grenzgeb., Band iii, Heft 9, p. 471.

<sup>3</sup> Clin. Therap. Woch., 1913, vol. xx, p. 198.

**Pituitrin as a Peristaltic Agent** has not as yet found wide-spread acceptance. Hill<sup>1</sup> reports a series of 800 abdominal operations in the after-treatment of which he used pituitrin. He found it useful both as a stimulant of the cardiovascular system and of the intestines.

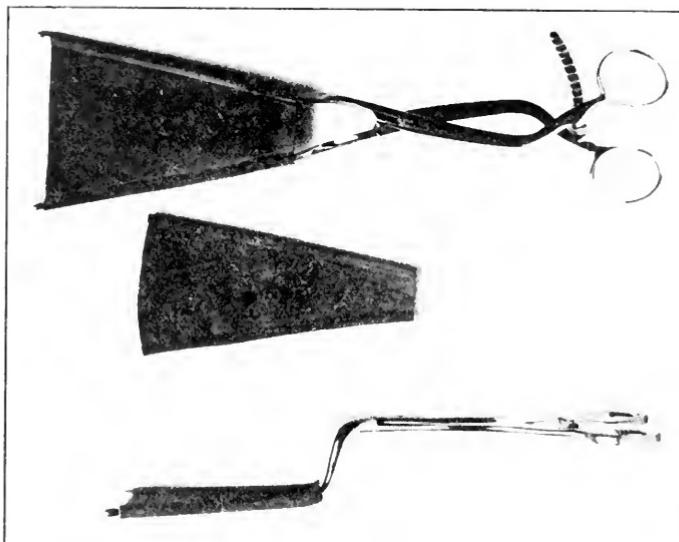


FIG. 37.—Abdominal depressor with rubber web. (Hadden.)

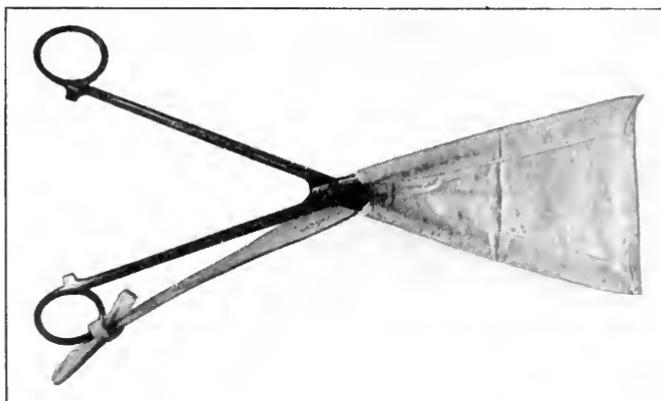


FIG. 38.—Blades of ordinary curved dressing forceps inserted into hems on sides of cloth triangle and tape tied to finger-ring. (Kahn.)

**Instruments.** VISCERAL DEPRESSORS. The instruments of Hadden,<sup>2</sup> Kahn,<sup>3</sup> and Ahlborn,<sup>4</sup> have the same general shape and produce the

<sup>1</sup> Boston Medical and Surgical Journal, May, 1913.

<sup>2</sup> Journal of the American Medical Association, vol. lx, p. 897.

<sup>3</sup> Ibid., vol. lx, p. 897.

<sup>4</sup> Ibid., vol. lxi, p. 2066.

same mechanical effect. This may be seen in the accompanying illustrations (Figs. 37, 38, and 39). The common tablespoon used by the Mayos for this purpose is simpler, cheaper and more effective. The hollow of the spoon makes allowance for the curve of the needle as it perforates the peritoneum.

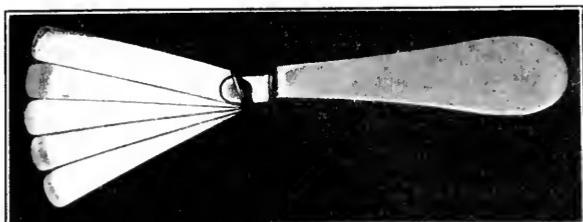


FIG. 39.—Ahlborn's visceral depressor.

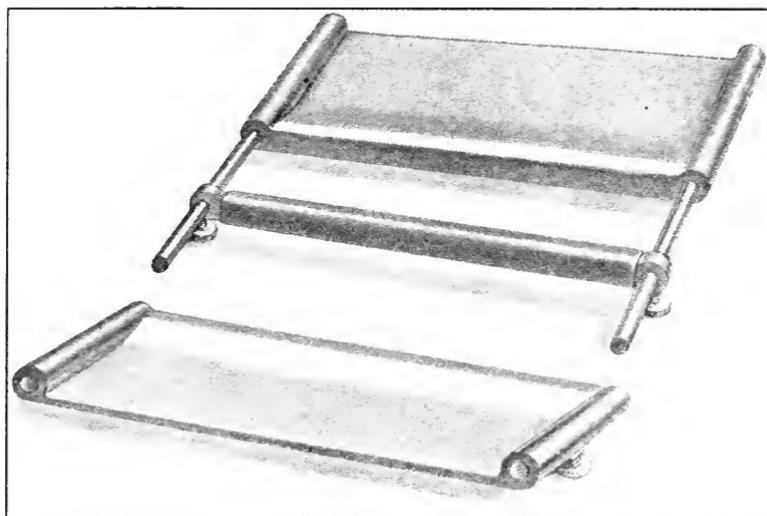


FIG. 40.—Bartlett's gastro-enterostomy clamp.

**BARTLETT'S IMPROVED GASTRO-ENTEROSTOMY CLAMP.** The accompanying illustration (Fig. 40) shows the mechanical details of the instrument. The two outside blades have been widened to hold the viscera and packs aside. The stomach is held between the fixed outside blade and the movable middle blade which is locked in position by the thumb screws underneath. In like manner the jejunum is fixed between the middle and lateral blades. After suture, the instrument is removed by unfastening the four thumb screws and withdrawing the fixed broad blade. This allows the other two blades to fall apart and they may be taken out separately.<sup>1</sup>

<sup>1</sup> Willard Bartlett, *Annals of Surgery*, November, 1913, p. 659.

In cases where the stomach and jejunum are readily delivered upon the surface of the abdominal wound, this instrument of Bartlett's is hardly necessary. Its true worth will be shown where the viscera cannot be delivered and where the necessity for holding the adjacent organs aside is most urgent; but in some of these cases it will be impossible to apply the instrument in a suitable manner because of its breadth.

The modifications of Bartlett's original instrument show great ingenuity in meeting the mechanical obstacles present in intestinal anastomosis, and this without losing the original simplicity. Still further improvements may confidently be expected.

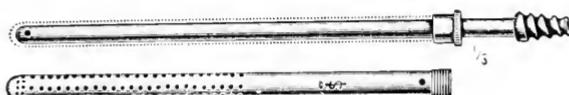


FIG. 41.—Straight tip without irrigating tube for aspiration in abdominal operations. (Pool.)

AN IMPROVED SUCTION TIP FOR ASPIRATION IN ABDOMINAL OPERATIONS. Kenyon's and Pool's aspiration apparatus was reviewed in PROGRESSIVE MEDICINE for June, 1911, page 75. Briefly, permanent suction is obtained from any suitable source, such as water-pressure or steam-pressure. From this source, a suction pipe of non-collapseable rubber hose leads to a gallon bottle under the operating table and from this bottle another pipe leads to the aspirating tip in the wound. The actual suction tip is separated from the viscera by an outer covering (see Fig. 41) having many fenestra. As there is a definite space between the inner aspirating tube and the outer protective one, it is impossible for viscera to reach the sucking orifices of the inner tube, consequently there is no danger of their being injured by too much suction. In a second communication Pool<sup>1</sup> announces that this apparatus has been in daily use at the New York Hospital for about six years, and has given complete satisfaction. When first brought out, curved and bent suction tips were made of various sizes. These were frequently combined with irrigating apparatus. The irrigating tubes have been eliminated as unnecessary, and a simple straight suction tip has finally proved most satisfactory. The present model (see Fig. 41) is of convenient size, and its strong construction enables it to withstand constant rough usage. When the instruments are prepared for operation, the suction tip and the tube leading from the bottle to the field of operation are boiled as a routine and are always ready for instant use. This convenient and simple apparatus ought to find wider adoption.

<sup>1</sup> Annals of Surgery, October, 1913, p. 537.

**Tuberculous Peritonitis.** The various methods by which this condition has been treated with more or less success were brought out in the discussion of Kümmel's paper<sup>1</sup> read in Hamburg early in 1913. Kümmel employs  $\alpha$ -ray treatment after laparotomy. Urban uses tuberculin after operation. Lauenstein enumerated the varieties of treatment which might be considered as aids to the operative treatment. Among these were radium, mesothorium, Finsen rays, Röntgen rays combined with ultraviolet rays, and the internal administration of tuberculin and quinine. Last, but not least, came the successful results of Rollier with sunlight, at Leysin.

I believe it was Murphy who suggested some time ago that the recovery of certain cases of tuberculous peritonitis after simple laparotomy might be due to agglutination of the hitherto open Fallopian tubes (the primary focus), the supposition being that the presence of fluid kept the tubes open and its removal allowed their fimbriated ends to adhere together, thus preventing the continuous reinfection of the peritoneal cavity which had been present up to this time.

**Various Abdominal Conditions Caused by Ascarides** were reported at the meeting of the "Mittelrheinische Chirurgvenvereinigung" on June 7, 1913.<sup>2</sup> Before recounting several of the more interesting cases presented, it might be well to refer to the review on ascarides in my last year's article in which it was shown that most pathological conditions associated with the presence of intestinal worms were due to the action of their poisonous secretions, not to the simple mechanical effect of their presence.

Hohmeier told of a boy, aged eight years, with a painful mass in the right iliac fossa supposed to be an appendix abscess. Upon opening the belly, a slight amount of free fluid escaped; the appendix was not involved; an irreducible ileocecal intussusception was present; the ileum above this mass was found filled with ascarides; the gut was spastically contracted at three distinct points where the worms had formed themselves into balls. Uneventful convalescence followed a resection with side-to-side anastomosis.

Schloessmann reported 6 instances in which the ascarides were found free in the abdominal cavity in the presence of a gangrenous appendicitis, and 2 cases of intestinal obstruction due to the worms—one a volvulus, one an obturation.

Bertelsmann operated on a spastic ileus in which the ileum was firmly contracted down upon a ball of worms at a point 50 cm. above the ileocecal valve. After kneading this mass so that it separated, the abdomen was closed and recovery followed under appropriate medication.

Schmidt showed the pancreas and liver of a woman, aged thirty-nine

<sup>1</sup> Zentralbl. f. Chir., 1913, p. 468.

<sup>2</sup> Ibid., p. 1175.

years, who had for two months after delivery suffered with abdominal cramps, vomiting, and icterus of varying intensity. Upon admission to the hospital, she had high fever, deep jaundice, and a large tender liver. Exploration showed the liver studded with hard nodes the size of cherries; the pancreas was thick and hard. The condition was considered a primary carcinoma of the pancreas with secondary deposits in the liver. The following day, however, an ascaris was present in the vomitus. In spite of the exhibition of santonin and castor oil, her fever continued, she gradually lost ground, and finally died. Autopsy revealed the bile passages crammed to their smallest branches with ascarides. The nodes seen at operation turned out to be abscesses containing ascarides. The main pancreatic duct contained a full-grown ascaris.

In this connection Beck reported a case of chronic ulcerative colitis of the cecum and ascending colon due to masses of trichocephalus, accompanied by severe anemia, thrombosis of both iliac veins and of the inferior vena cava. Improvement followed the evacuation of the parasites, establishment of a cecostomy, and 1 per cent. thymol irrigations. At the end of six months, the thrombosis of the inferior vena cava spread to the renal veins and was followed by death from uremia.

**The Great Vessels of the Abdomen.** (a) EMBOLUS OF THE ABDOMINAL AORTA; REMOVAL; RECOVERY. Bauer's<sup>1</sup> patient was a man, aged thirty-nine years, who had suffered from articular rheumatism for sixteen years. Examination led to the diagnosis of mitral insufficiency and stenosis. While in the hospital for treatment of his cardio-rheumatic condition, suddenly there were excruciating pains in both legs, especially the left; he was unable to move them, and noticed that they had become blue and cold. Examination two hours later showed absence of pulse in both femoral arteries. The skin of both legs and of the abdomen up to the umbilicus was cyanotic and cold; there was complete anesthesia of the feet and legs, and diminished sensation over the thighs and lower abdomen. The lower limbs could not be moved. In the absence of abdominal symptoms, embolism of the abdominal aorta close to its bifurcation was diagnosed.

The abdomen was opened three hours after the onset of symptoms; a median incision 20 cm. long permitted ready eventration of the entire small intestine. The posterior peritoneum was incised to the left of the root of mesentery and the aorta and common iliacs were exposed for a distance of 10 cm. The aortic pulse extended to within 3 cm. of the bifurcation; here a mass was felt to occupy the aortic lumen, extending a little down the iliacs. An assistant digitally compressed the aorta above; the embolus was easily extracted through

<sup>1</sup> Zentralbl. f. Chir., 1913, No. 51, p. 1945.

a longitudinal incision of 2 cm. Closure of the vessel wall with fine silk. Hemorrhage from the suture line, upon release of digital compression above, was controlled (as is customary in all arterial suturing) by a few minutes' local compression of the suture line. (Such compression is very light so as not to interfere with the newly established stream through the vessel's lumen.) The pulse in the iliacs was promptly reestablished; the intestines were replaced, and the abdomen was closed. Convalescence was uneventful.

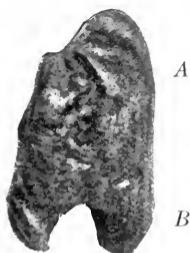


FIG. 42.—Embolus removed from bifurcation of abdominal aorta. *A*, in abdominal aorta; *B*, in iliac arteries.

The specimen was 3 cm. long, having the form of a molar tooth (Fig. 42); upon section a grayish-yellow nucleus of firm consistency as large as a hazelnut (probably the original embolus) was found surrounded by a mass of red coagulum.

(b) TEMPORARY EMBOLISM OF THE SUPERIOR MESENTERIC ARTERY. A woman with cardiac disease was suddenly seized with abdominal pain. There was subnormal temperature, and a small, frequent pulse. Bornstein<sup>1</sup> opened the abdomen two hours after the onset of symptoms. A quantity of clear, yellow serum escaped; the small intestine and ascending colon were very anemic and tightly contracted. During manipulation of the intestines, their color suddenly returned and they relaxed. Exploration of the abdominal viscera failed to show any other abnormality; the appendix was removed. Upon coming out of the anesthetic, intense pain was felt from the left knee downward. The leg and foot were cold and cyanotic. In a short time dry gangrene set in; the line of demarcation lay above the ankle-joint.

On the fifteenth day after operation the left leg was amputated at the knee-joint. An acute postoperative dilatation of the stomach was relieved by stomach washing. Otherwise convalescence was uneventful. At no time were there symptoms referable to the intestines.

A few days later while talking with her husband, the patient suddenly fell over in bed and died. There were a few convulsive movements of the left side of the body. Permission for autopsy was not granted.

Bornstein believes that an embolus blocked the mouth of the superior

<sup>1</sup> Journal of the American Medical Association, vol. ix, p. 513.

mesenteric artery and became dislodged during manipulation at laparotomy when it was carried down to the popliteal artery, where it lodged again. Death in all probability was due to cerebral embolism.

(c) RUPTURE OF THE INFERIOR VENA CAVA from an accident: suture of the vessel.<sup>1</sup>

A man, aged forty years, had been run over by an automobile. At laparotomy, the lacerated right kidney was removed. The hemorrhage, which still persisted, was found coming from a longitudinal tear 1 cm. long in the inferior vena cava. After temporary closure with hemostats, closure of the vessel wall was made with fine interrupted sutures of silk. Following operation the patient did not do well, and finally died of pulmonary tuberculosis six weeks later. At autopsy the vena cava showed a linear scar at the site of the former tear.

### THE STOMACH.

**Postoperative Dilatation of the Stomach** was considered in PROGRESSIVE MEDICINE, June, 1911, pages 101 to 105. There is still disagreement about the exact etiology of this condition. Of all the articles appearing since the previous review, the most important is that of von Haberer.<sup>2</sup> This author differentiates between a primary dilatation of the stomach with secondary duodenal obstruction<sup>3</sup> and a primary duodenal obstruction of its third part (arteriomesenterial ileus), following which there may or may not be a secondary gastric dilatation. Von Haberer considers that there is a distinct difference in the symptoms and course of the two conditions.

In acute primary dilatation of the stomach, the onset is gradual; if vomiting is present, it is not active but rather a simple regurgitation of gastric contents. This condition readily proves amenable to simple lavage and postural treatment.

On the other hand, arteriomesenterial ileus, according to von Haberer, is due to fixation of that portion of the small intestine lying in the true pelvis, thus narrowing or even obliterating the angle of the superior mesenteric artery with the vertebral column, thereby constricting the third portion of the duodenum. This causes a typical, acute intestinal obstruction high up in the alimentary canal. The onset is sudden, with profound prostration and a small, rapid, high-tension pulse. Usually there is repeated projectile vomiting. If, on the other hand, the mucosa at the cardia acts as a valve, the stomach fills up

<sup>1</sup> Schmieden, Deutsch. Zeitsch. f. Chir., Band exxii, p. 591.

<sup>2</sup> Ergebnisse d. Chir. u. Orthopädie, 1913, Band v, p. 467.

<sup>3</sup> In primary dilatation, after the stomach has reached a certain size, it presses the transverse part of the duodenum against the vertebral column, thereby obstructing it.

to an alarming extent within a very short time. Autopsy on cases dying with the first of these two clinical pictures (with projectile vomiting) shows a non-dilated stomach with a patent pylorus stretched to the same size as the dilated duodenum whose dilatation ends abruptly at its crossing with the superior mesenteric artery.

*Treatment.* Naturally, these cases do not prove amenable to frequent gastric lavage. On the other hand, knee-elbow or right-sided postures allow the intestines (if they are movable) to escape from the small pelvis and relieve the obstruction in a prompt, almost magical way. In von Haberer's cases where frequent lavage, plus postural treatment, failed to bring relief, operation or autopsy revealed firm adhesions, fixing the small intestine in the true pelvis. In other words, if this condition is not relieved within a few hours by lavage and by postural methods, laparotomy should promptly follow before the patient becomes too exhausted.

It is well to remember that packings inserted at operations upon the gall-bladder or right kidney have caused duodenal obstruction (gastric dilatation); prompt relief has followed their withdrawal.

**Acute Dilatation of the Stomach Occurring during Operation** is reported by W. G. Richards.<sup>1</sup> Operation was performed seven hours after the perforation of a duodenal ulcer. The perforation lay half an inch from the pylorus and was closed by suture. No gastro-enterostomy was made. While the peritoneum of the laparotomy wound was being closed, suddenly the stomach became enormously distended so that its veins stood out like black cords. A stomach tube was hurriedly passed and a large quantity of gas escaped; then the stomach contracted to the size of the large intestine. The patient made an uneventful recovery. Richardson ascribes this phenomenon to some central nervous disturbance. Since, according to the history, a difficult ether anesthesia was being given to an alcoholic subject, a more obvious explanation would be that the struggling, semiconscious patient swallowed a small quantity of ether which rapidly became vaporized in the stomach.

**Gastroscopy.** Ever since its inception, the value of information to be obtained by this means has never been underestimated. The method's two great drawbacks have been: (1) The danger of perforation of the esophagus by the instrument, which, when it occurred, almost invariably led to a speedy death; (2) the great discomfort it caused the patient. For these reasons it has remained in the hands of a few investigators, like Chevalier Jackson, who have made this field their special study. Taking these factors into consideration, H. H. Janeway<sup>2</sup> suggests avoiding the discomfort by conducting examination

<sup>1</sup> British Medical Journal, November 8, 1913, p. 1202.

<sup>2</sup> Journal of the American Medical Association, October 11, 1913, vol. lxi, No. 15, p. 1339.

under nitrous oxide intratracheal anesthesia, instead of ether, and further, insists that no danger from perforation can occur if the instrument be inserted under the constant guidance of the eye. The point of the esophagoscope must not be advanced until the folds of mucous membrane in front of it are actually seen to fall away under air distention.

**Jianu's Method of Gastrostomy** has come into special prominence in connection with the recent advances in the radical cure of cancer of the thoracic portion of the esophagus. It is the simplest and safest of all the operations so far devised for fashioning an artificial esophagus from the stomach, small or large intestine. The entire subject is summarized in a brief, clear manner by Willy Meyer.<sup>1</sup> The indications for performing this operation belong to the domain of thoracic surgery. I shall therefore limit myself to a brief description of the technique.

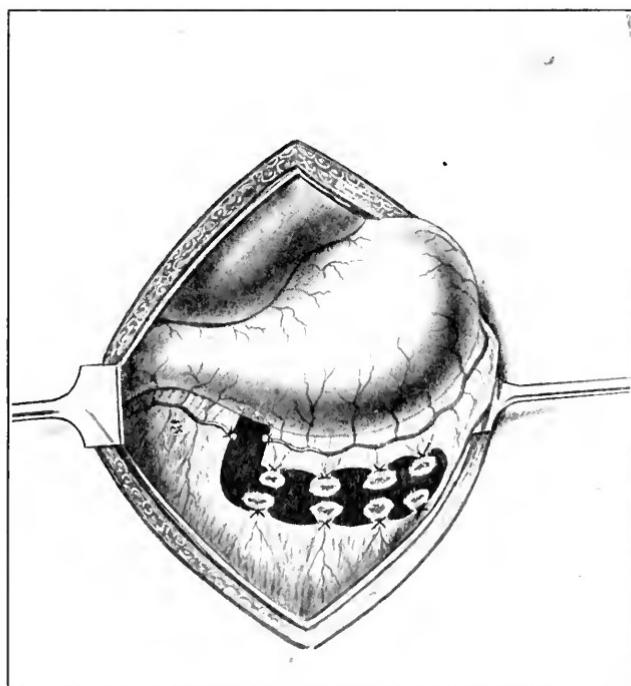


FIG. 43.—Jianu's gastrostomy and inferior esophagoplasty. Median incision; double ligation and division of greater omentum up to the point at which left inferior epiploic artery reaches the stomach. Double ligation and division of right inferior epiploic artery; exposure of greater curvature of stomach. (Meyer.)

The stomach is delivered through a median epigastric incision, the great omentum is divided between ligatures from a point about two

<sup>1</sup> Journal of the American Medical Association, January 10, 1914, p. 100.

inches from the pylorus, around to the left where the left inferior epiploic artery turns to join the stomach. At the right end of this omental opening, the right inferior epiploic artery is divided between ligatures, thus exposing the greater curvature of the stomach at this point (Fig. 43).

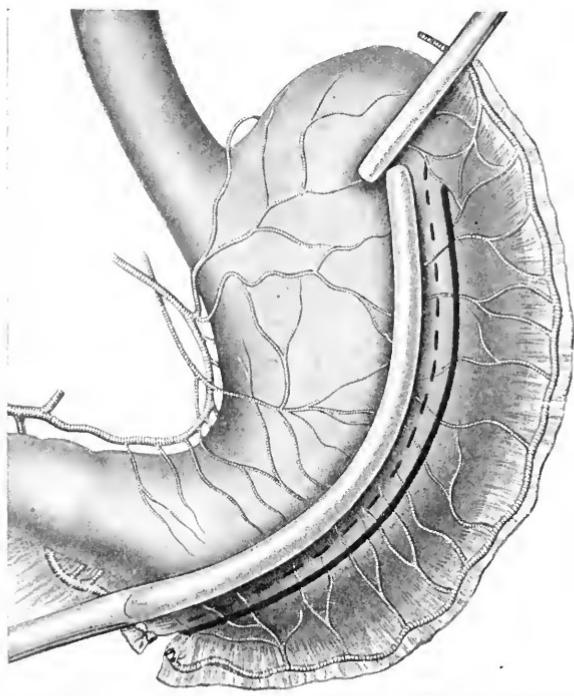


FIG. 44.—Employment of clamps to prevent leakage while fastening the Jianu tube. (Meyer.)

Beginning here, a mattress suture approximating the anterior to the posterior wall of the stomach, runs parallel to the greater curvature about one and a half inches away from it. Meanwhile the stomach is lifted up by an assistant in order to displace its contents toward the lesser curvature; at this stage the appropriate employment of curved or straight clamps (Fig. 44) will prevent leakage. That part of the greater curvature now isolated from the rest of the stomach by suture is cut away up to the point where the mattress suture ends, namely, where the vas brevia join the stomach. A Connell continuous mattress suture begins where the isolating mattress suture of the greater curvature ends and running upward on the pedunculated flap of gastric wall, forms it into a Jianu tube (Fig. 45). A second continuous suture is then made, beginning from the start of the first mattress suture near the pylorus, up to the end of the Jianu

tube. The end of the tube is temporarily inverted by two or three sutures, ends of which are left long.

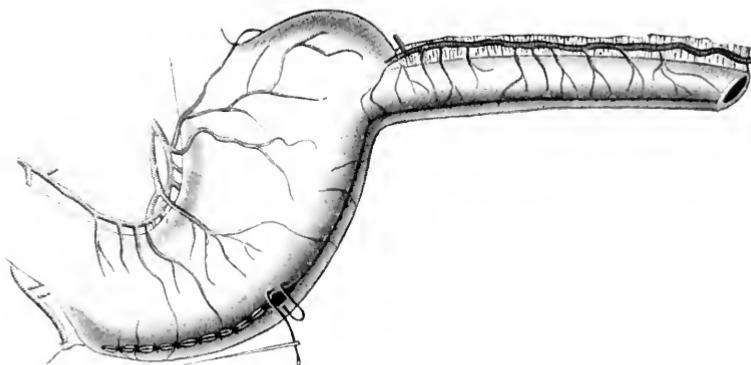


FIG. 45.—The major curvature flap formed into a tube—Jiani tube—by means of a continuous Connell suture; a second running suture (preferably Cushing's) secures the first row. (Meyer.)



FIG. 46.—The second case, male, sixty-eight years old, operated upon at the German Hospital, with the help of Hürtl's wire-stitching instrument. (Meyer.)

The stomach is now turned so that the base of the Jiani tube corresponds to the upper angle of the abdominal wound; here it is secured by a few stitches. The Jiani tube is placed on the chest to the left of

the sternum; a horizontal skin incision is made at the point reached by the upper end of this tube, which is then laid aside. By blunt dissection, a subcutaneous passage is now established between the upper end of the laparotomy wound and the transverse, horizontal skin incision on the thoracic wall. A long clamp, passed through this tunnel from above downward, grasps the long ends of the inverting sutures, and draws the Jianu tube up to its proper place. The inverting sutures are now removed and the mucosa of the tube is sutured to the margins of the skin wound. (These anchoring sutures should not pass through all three coats of the new tube, for fear of marginal necrosis.) A small bit of gauze is placed in either corner of the wound for temporary drainage; and the orifice of the tube is lightly packed with a little gauze. The abdominal wound is closed.

The Jianu method affords a tube of ample caliber with good blood supply, 18 to 25 cm. long, completely surrounded by peritoneum. The Jianu operation should be employed solely for the purposes of esophagoplasty. As a simple gastrostomy, it is unsatisfactory, because, in spite of the length of the tube, gastric contents often escape from its mouth. The accompanying illustration shows (Fig. 46) one of Meyer's three successful cases.

**GASTROSTOMY.** A disadvantage of the usual gastrostomy is, that even a few hours' neglect to wear the tube in place often renders reintroduction impossible. On the contrary, a gastric fistula lined with epithelium instead of with granulation tissue, will remain patent. Janeway<sup>1</sup> has devised such a fistula. First, he tried it on dogs and it proved satisfactory. There was no leak even during vomiting or barking. Later, in five patients with inoperable carcinoma of the esophagus, the fistula proved equally useful. The method is similar to but less extensive than that of Depage.

The operation may be performed under local anesthesia. It requires an abdominal incision of only 3 cm.; this is made parallel with the muscle fibers over the inner third of the left rectus a short distance below the costal cartilage. The fibers of the muscle are bluntly separated. Upon opening the peritoneum, the anterior wall of the stomach is pulled up through the wound and held over to the left by two clamps (Fig. 47). A horizontal incision 3 to 4 cm. long is then made between the two clamps. Two short perpendicular incisions 1 cm. long extending toward the greater curvature are then made at each extremity of the first cut (Fig. 48). The flap *C'A'B'D*, is created by these incisions (Fig. 49); it is then folded back (Fig. 50) and *X* is pulled upon (Fig. 51). The opposite margins indicated by the letters *A'C'A'* and *B'D'B'* are approximated, and when sewed together, form a tubular canal (Fig. 52).

In this manner a canal at least 5 cm. long is created without dimin-

<sup>1</sup> Journal of the American Medical Association, vol. lxi, No. 2, p. 93.

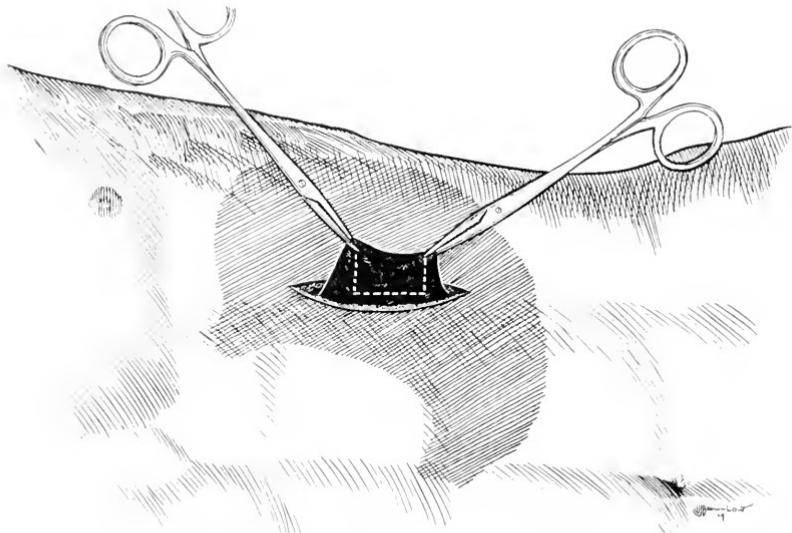


FIG. 47.—Anterior stomach wall drawn out of abdominal wound by two clamps (Janeway's gastrostomy).

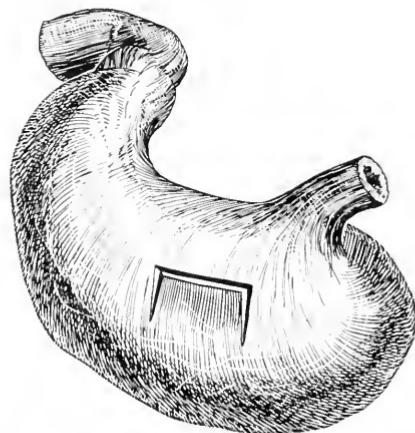


FIG. 48.—Diagrammatic representation of gastrostomy incisions.

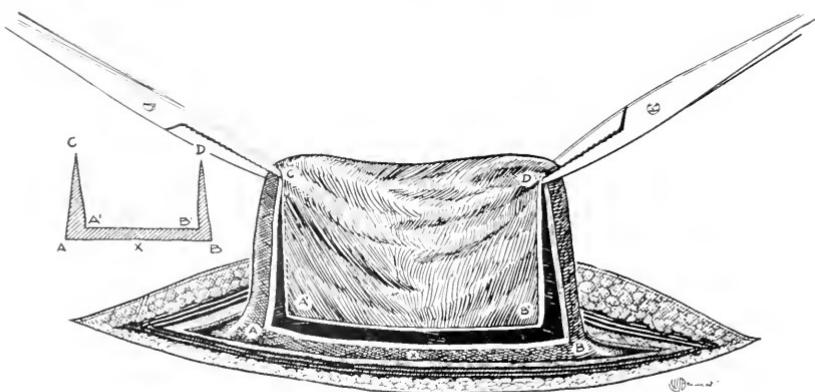


FIG. 49.—Immediately after incisions have been made.

ishing the transverse diameter of the stomach. Near its base, this canal is then sutured to the parietal peritoneum and to the posterior sheath of the rectus. Its apex is attached to the skin of the abdominal wall. An essential feature of Janeway's operation is the oblique direction

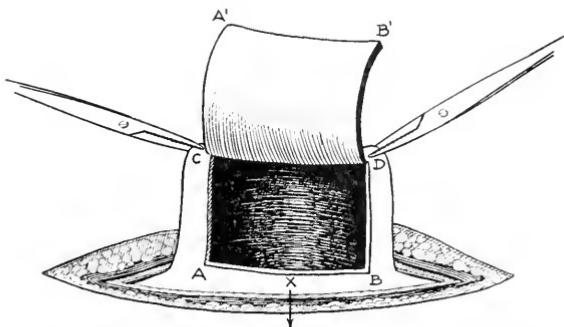


FIG. 50.—Flap  $C'DA'B'$  turned back. Arrow indicates direction in which  $X$ , midway between  $A$  and  $B$  is to be drawn. This will cause the margins of the openings to assume the shape shown in Fig. 51.

given to the new canal. In order to accomplish this, a spot on the stomach wall, somewhat to the right of the abdominal incision, is selected. The tubular canal, after its formation, has an oblique direction to the left. According to Janeway, any increase of intragastric

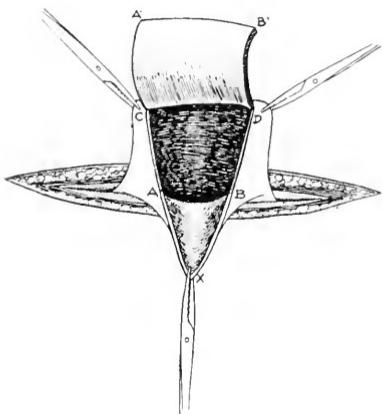


FIG. 51.—Beginning at  $X$ , the sides of the opening are approximated by suture so that  $A$  and  $B$  and  $C$  and  $D$  come together; the suture continuing, without interruption, unites the margins  $C A'$  and  $D B'$ , so that the flap  $C A' B' D$  forms a tube with its outer orifice at  $A' B'$ .

pressure will bring the walls of the fistula together and will effectually prevent escape of stomach contents.

*Closure of a Gastrostomy Fistula.*—Last year I reviewed von Hacker's method of closing a gastrostomy fistula by means of two subcutaneous

silver wire loops. In a second publication von Hacker<sup>1</sup> announces that he uses strips of fascia instead of silver wire for this purpose.

**Congenital Hypertrophic Pyloric Stenosis.** The importance of arriving at an early accurate diagnosis of this condition is emphasized by Seudder.<sup>2</sup> In his first 12 operative cases there were no deaths. In the last 4, there were 3 deaths due to the exhausted condition of the children when they were submitted for operation.

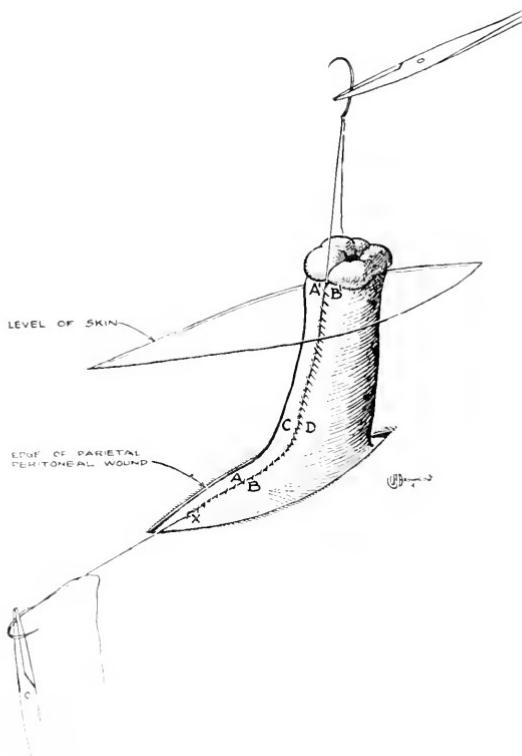


FIG. 52.—Gastrostomy tube completed.

As I have said elsewhere in this article, the *x*-ray has proved of great value in arriving at a timely, accurate diagnosis of this condition as well as in differentiating it from clinically similar cases in which the symptoms are due to other causes, and in which, consequently, an operation is not indicated. Up to the present time, the usual procedure has been to establish a gastro-enterostomy. *X*-rays taken as late as three years (Mixter<sup>3</sup>) and five years (Seudder) after operation have shown the persistence of the pyloric stenosis with entire passage of food through the

<sup>1</sup> Zent. f. Chir., 1913, p. 659.

<sup>2</sup> Annals of Surgery, February, 1914, p. 239.

<sup>3</sup> Boston Medical and Surgical Journal, 1913, No. 9.

stoma of the gastro-enterostomy. Scudder cites the postmortem of a case in which the patient died seven and one-half months after gastro-enterostomy; the pyloric tumor was still present.

Scudder, moreover, refers to a list of individuals who had managed to survive until adult life in spite of the handicap of congenital pyloric stenosis. One of these was the case of Barling referred to last year on page 98 of my article.

Scudder speaks of early diagnosis and prompt operation as a means of reducing the mortality from 50 per cent. to 13 per cent. I believe that substitution of Rammstedt's<sup>1</sup> simple division of the pyloric muscle down to the mucosa for gastro-enterostomy hitherto employed, will still further reduce the mortality in many of the far-gone cases. Early in this year Lilienthal<sup>2</sup> did such an operation on a two weeks old baby. The operation was done with ease, simplicity, and speed. The child made a prompt and uneventful recovery. A. S. Taylor has had a similar case.

**Interrelation of Stomach and Small Intestine.** By establishing fistulas at various points along the gastro-intestinal tract of the same animal, Baumstark<sup>3</sup> has shown, that when normal products of gastric digestion are introduced into the small intestine, a normal sequence of events occurs in the stomach—the stomach secretes gastric juice and discharges its contents in a normal manner. On the other hand, the introduction of partly fermented, or putrid, food mixtures into the small intestine causes a great delay in the discharge of test-meal contents of the stomach. This is a strong proof of the production of gastric disturbances by fermentative changes in the bowels. Thomson,<sup>4</sup> working along the same lines, found that the presence of an abundance of sugar in the intestine may delay the discharge of the contents from the stomach (see also remarks of Hertz below, under Unfavorable After-effects of Gastro-enterostomy).

**Gastropasm.** The instructive article of Holzknecht and Luger<sup>5</sup> includes a series of 16 cases. The authors distinguish between gastropasm, where there is absence of peristalsis, and hypertonicity of the stomach, where exaggerated peristalsis is often seen. Furthermore, in hypertonicity, the entire organ is affected, while in gastropasm one must distinguish between circumscribed forms (spastic hour-glass stomach), regional forms (especially affecting the pyloric part of the stomach), and total gastropasm. The motility of the stomach undergoes marked variations: either it may be increased, probably on account of pyloric insufficiency, as, for example, in duodenal ulcer; or, it may be delayed in the presence of biliary disease

<sup>1</sup> For Rammstedt's operation see PROGRESSIVE MEDICINE, June, 1913, p. 98.

<sup>2</sup> Personal communication.

<sup>3</sup> Zeitsch. f. physiolog. Chemie, 1913, vol. LXXIV, p. 437.      <sup>4</sup> Ibid., p. 425.

<sup>5</sup> Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1913, Band xxvi, Heft 4, p. 669.

or in the marked hypertonicity of the morphine habit. The diagnosis is made by the lack of constancy in pictures taken at different times and by the subsidence of the spasm under the influence of atropin or of papaverin. In one instance, the spasm relaxed and the stomach assumed its normal shape during the ten or fifteen minutes the patient was being examined. In still another, the stomach appeared normal at first; an hour later there was total gastospasm, and still an hour later it had entirely subsided. In 4 cases the findings were entirely different on different days. In certain individuals, atropin caused the spasms to relax; thus in one instance the stomach did not empty itself for twenty-four hours, but, after the administration of atropin, it completely emptied itself at the end of two hours. The interpretation of this was, that the atropin had caused the pylorus to relax, although the general gastospasm still persisted to a certain extent, resulting in rapid emptying of the stomach.

Examples of partial gastospasm (hour-glass stomach) secondary to extraneous conditions are given by A. E. Barclay.<sup>1</sup> Repeated x-ray examinations showed that the spasmodic contraction was present on some days and absent on others. Operation revealed no sign of a pathologic change. In almost every case, the patient either had carious teeth, or was suffering from an obstinate constipation. When these sources of chronic intoxication were removed, the gastric symptoms promptly ceased.

Barclay has observed that as soon as the oral sac of a spastic hour-glass stomach is emptied by vomiting, the pain and nausea cease. In two specially significant cases with carious teeth, the stomach retained the entire amount of food ingested for longer than twenty-four hours; after removal of the diseased teeth, the stomach was found empty at the end of five hours. Such conditions as mucous colitis and appendicitis have also been found to cause spasm of the stomach.

Barclay believes that such spasmodic narrowings of the stomach predispose to injury of the mucosa from large irregular masses of insufficiently chewed material; the continuation of this spasm, which may be interpreted as an effort to hold the large pieces of food in the stomach until they have been properly disintegrated, naturally insures a prolonged action of the gastric juice. If to this be added fresh traumata from additional ingress of poorly masticated food, it is not difficult to perceive how an ulcer may become established. In many cases, as we know, the presence of an ulcer is the cause of a local gastospasm, and so a vicious circle is established which can no longer be cured by the removal of bad teeth or the correction of chronic constipation.

**Ulcer. EXPERIMENTAL GASTRIC ULCER.** In the course of a fascinating address upon the lesions produced by the streptococcus group,

<sup>1</sup> Proceedings of the Royal Society of Medicine, 1913, vol. vi, No. 7, p. 138.

delivered on November 18, 1913, at the New York Academy of Medicine, Rosenow, of Chicago, announced the fact that streptococci had been gained from the walls of chronic gastric ulcers obtained at operation, and that these strains of streptococci, when injected into dogs, showed as distinct and definite an affinity for the gastro-intestinal mucosa, as strains of streptococci isolated from rheumatic lesions, showed for the joints and muscles. Many of the dogs injected with the streptococci obtained from human gastric ulcers, died within two weeks from perforation of, or hemorrhage from, fresh ulcers of the stomach.

This is the most important contribution to the etiology of gastric ulcer that has been made in years. However, it is only one aspect of a vast and many-sided discovery which has attracted universal attention. Its further developments are being awaited with the keenest interest and expectation.

Steinhärter,<sup>1</sup> of the Cincinnati General Hospital, working along different lines was also constantly able to produce experimental gastric ulcers.

Colon bacilli, caused to agglutinate by being placed in weak solutions of acetic or of hydrochloric acid, were then washed in salt solution and injected into the vein of a rabbit's ear. Within twenty-four hours after the injection of 2 to 3 c.c. of such an emulsion, gastroduodenal ulcers were invariably found.

**LOCATIONS IN WHICH GASTRIC ULCERS ARE NOT DEMONSTRABLE UNDER THE X-RAY.** Friedenwald and Baetjer<sup>2</sup> point out the difficulty of demonstrating lesions of the posterior wall of the stomach by *x*-ray. Only when a lesion is situated on the anterior surface, or along the anterior surface of the lesser and greater curvatures, is it at all demonstrable.

**SYMPOTMS.** The recent articles of Smithies<sup>3</sup> summarize, up to date, the clinical experience of the Mayo clinic in this field. These comprehensive collections of facts do not lend themselves readily to condensation.

**THE SURGICAL TREATMENT OF GASTRIC ULCER.** According to the dictum established by the Mayos, callous ulcer of the stomach should be excised whenever possible because of the likelihood of cancer developing on the base of the ulcer.

**Resection.** Kümmell,<sup>4</sup> of Hamburg, in speaking of callous ulcers of the pylorus, does not believe that cancer develops in them as frequently as has been maintained. Among a relatively large number of cases, he has only observed one instance in which carcinoma developed upon an ulcer after gastro-enterostomy. On the other hand, he has seen the development of carcinoma after resection of a callous ulcer of the

<sup>1</sup> Boston Medical and Surgical Journal, 1913, p. 81.

<sup>2</sup> American Journal of Medical Sciences, October, 1913.

<sup>3</sup> Journal of the American Medical Association, vol. lxi, p. 1793. American Journal of the Medical Sciences, 1913, vol. exlv, p. 340.

<sup>4</sup> Zentralbl. f. Chir., 1913, p. 1994.

pylorus which, upon microscopic examination, failed to show any malignant change.

For ulcers involving the central part of the stomach, especially those along the lesser curvature, Kümmell has found satisfaction in employing *transverse resection* as first suggested by Riedel. Of his 18 cases in which this operation was performed, Kümmell was able to follow nine. Clinically, these patients were entirely cured; their gastric functions gave them no trouble whatever, and they had no difficulty in following their vocations. *x-ray* examination of these patients showed an hour-glass stomach, the two halves of which were joined by a narrow passage. In one instance, this passage was seen to widen as more food was ingested. The motility of the stomach and small intestine was increased, the bismuth mixture leaving the stomach and reaching the cecum within a very short time after being swallowed.

In discussing a paper by Hedlund in which the late results after resection for ulcer were shown to surpass those after gastro-enterostomy, Krogius,<sup>1</sup> of Helsingfors, stated that whenever possible, he resected, as he had had the disagreeable experience of losing 5 patients from subsequent complications due to ulcers for which gastro-enterostomy had been done.

Borelius then demonstrated the stomach obtained at autopsy from a patient upon whom he had performed gastro-enterostomy fifteen months before for callous pyloric ulcer with its base perforating the pancreas. The ulcer was completely healed.

Until we know the exact conditions which in one case bring on cure of a callous ulcer, and in another, cause a cancer to develop upon its base, excision (resection), whenever this is technically possible, and occlusion when it is not, will remain the methods of choice.

Paterson,<sup>2</sup> of London, at the International Congress last year (August 12, 1913), considered occlusion of the pylorus an unnecessary complication of gastrojejunostomy, excision of simple ulcers unnecessary, and malignant degeneration of gastric ulcers after gastro-enterostomy, a rather rare occurrence.

**Gastro-enterostomy. INJURY TO THE COLICA MEDIA ARTERY IN POSTERIOR GASTRO-ENTEROSTOMY.** Cuneo<sup>3</sup> reports injury of the artery during suture of the opening in the transverse mesocolon to the stomach. The artery and vein had to be tied. The circulation of the transverse colon was not affected. In a second case, in the course of a resection for carcinoma of the pylorus, the gastro-epiploica dextra was seized in a ligature, together with a second artery which closer examination proved to be a colica media having an anomalous origin from the gastroduodenalis. Here, too, ligature of the artery did not affect the circulation of the transverse colon.

<sup>1</sup> Zentralbl. für Chir., 1913, p. 1631.

<sup>2</sup> Journal of the American Medical Association, vol. lxi, p. 798.

<sup>3</sup> Bull. et mém. de la Soc. Chirurg. de Paris, 1913, vol. xxxix, p. 174.

In discussing this communication, Ombredanne reported tearing of the ileo colica dextra close to its origin. Ligature of the artery did not cause gangrene of the gut.

An ingenious METHOD OF ESTABLISHING ENTERO-ENTEROSTOMY FOR THE RELIEF OF VICIOUS CIRCLE following posterior gastrojejunostomy has been devised by Willard Bartlett.<sup>1</sup> Upon reopening the abdomen, the operative field was found to be so deeply situated, and therefore technically so inaccessible for suture, that Bartlett invented another method of short-circuiting the duodenum. Making an incision in the anterior wall of the stomach, the gastro-enterostomy opening in the posterior wall was exposed. By means of a hysterectomy clamp, one-half of a Murphy button was introduced through this opening in the posterior wall into the duodenum (Fig. 53); then the other half of the button was introduced into the jejunum. Two small incisions were made through the intestinal wall exposing the neck of each half of the button. The two portions of the bowel were then joined by telescoping the halves. The patient made an uneventful recovery.

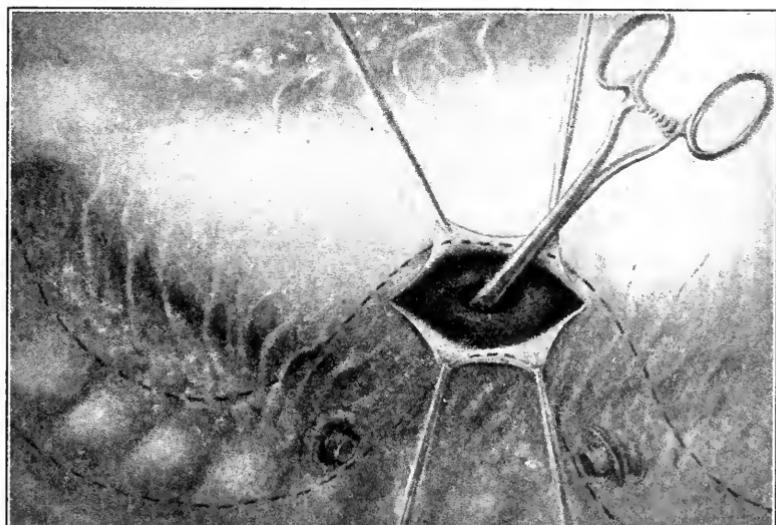


FIG. 53.—The two halves of a Murphy button have been introduced by the transgastric route, caught the two portions of bowel contiguous to the gastro-enterostomy opening and will be telescoped in order to short-circuit the loops for the treatment of vicious circle. (Bartlett.)

CONTRACTION OF THE STOMA AFTER GASTRO-ENTEROSTOMY WITH A MURPHY BUTTON. Certain authors have claimed that there is more danger from cicatricial stenosis of the opening made with the Murphy button than after suture. Cackovic<sup>2</sup> reports such a case. The patient

<sup>1</sup> Annals of Surgery, January, 1913, p. 81.

<sup>2</sup> Zentralbl. für Chirurgie, 1913, p. 1688.

was operated upon in 1906 by Murphy himself, following which his suffering was only temporarily relieved. At re-laparotomy, performed by Cackovic, the posterior gastro-enterostomy was found markedly contracted and an anterior gastro-enterostomy with entero-anastomosis was then done.

THE RECOGNITION AND TREATMENT OF CERTAIN UNFAVORABLE AFTER-EFFECTS OF GASTRO-ENTEROSTOMY. It is not uncommon for patients with a gastro-enterostomy to complain of a certain amount of discomfort after meals. In a series of about 20 cases operated upon by almost as many different surgeons, Hertz,<sup>1</sup> by means of the *x-ray*, was able to discover and remedy the causes of postprandial distress, thus converting partial into complete success. There were two separate groups.

1. *Too Rapid Drainage of the Stomach.* According to Hertz, the patient complains of a sensation of fulness which occurs during each meal and which may be so unpleasant that the amount of food taken is progressively diminished and a considerable loss of weight may follow. This sensation disappears rapidly and the patient may find that by eating with extreme slowness, he is able to prevent its occurrence. Many patients recognize that this sense of fulness is located slightly lower than the position where pain or discomfort was felt previous to operation.

In some cases there is a slight diarrhea, the bowels being moved after each meal. The first stool passed in the day is solid, but the later ones are unformed and occasionally fluid. Occasionally diarrhea may be severe. In one instance, a patient dying from diarrhea after gastro-enterostomy was autopsied and no organic cause of death could be discovered.

In all patients suffering from this group of symptoms, Hertz found, by means of the *x-ray*, that the stomach was small and hypertonic and that the passage of food out of it was extremely rapid, so that a bismuth meal left the stomach in less than an hour, and, in one case, in less than ten minutes after being taken, instead of requiring a normal three or four hours. The outflow from the stoma may appear almost as soon as food enters the stomach (Fig. 54). In all cases little or nothing passes through the pylorus, and sometimes the chyme even fails to reach the portion of the pyloric end of the stomach beyond the stoma. The rapidity of escape through the stoma does not depend upon the condition of the pylorus; for, in most of the cases seen by Hertz, the pylorus was left patent at operation; in fact, the most marked case Hertz observed was one in which the stomach was completely emptied less than ten minutes after a bismuth meal had been begun. Here at a second operation performed before Hertz had seen the patient, the

<sup>1</sup> Annals of Surgery, October, 1913, p. 466.

pyloric passage had actually been widened (by pyloroplasty), on account of persistence of symptoms.

Hertz believes that the rapid passage of gastric contents through the stoma leads to distention of the proximal part of the jejunum in a way which never occurs normally, and this distention of the jejunum is the cause of the sense of fulness. As proof of this, he cites his previous experiments showing that distention, which leads to stretching of the muscle fibers, is the only adequate stimulus of visceral sensation. Moreover, the situation of the sensation is lower than that due to gastric distention; further, these patients find that exercise or a dose of castor oil, which are known to increase the activity of the small intestine, exaggerate the discomfort but shorten its duration. The quantity, not the quality, of food ingested is the essential causative feature.

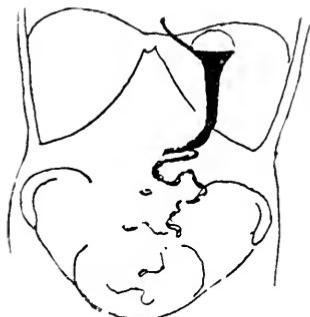


FIG. 54.—Five years after gastro-enterostomy for small duodenal ulcer, which did not produce obstruction. (Hertz.)

Regarding diarrhea, Hertz says: "It is mainly due to irritation of the bowels by the food which escapes too rapidly from the stomach for efficient gastric digestion; owing to the absence of the normal stimulation of the pancreatic secretion by hydrochloric acid in the duodenum, it does not undergo sufficient compensatory digestion in the intestines." The diarrhea "tends to occur after meals because of the normal gastrocolic reflex, which I have shown leads to an increase in the peristalsis of the colon whenever food enters the stomach. In all probability there is also an enterocolic reflex which arises from distention of the jejunum and produces the same effect." (See Interrelation of Stomach and Small Intestine.)

*Treatment.* By varying the position and watching its effect upon the stomach's rate of evacuation with the *x-ray*, one may ascertain the attitude which delays the unduly rapid emptying. In any case, the patient is made to recline after meals—experience determines which side it is best to lie upon. In addition to this, some active preparation of pancreatic ferment should be given to compensate for the deficiency

of the normal secretion, and, if the sense of fulness is still experienced, small doses of belladonna and codein have been recommended. If all these measures are ineffectual, Hertz suggests a secondary operation for either diminishing the size of or closing the stoma and reestablishing the original course of the food.

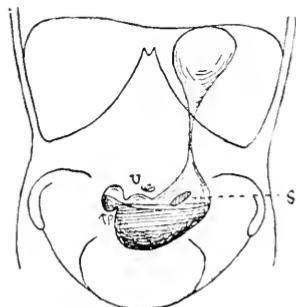


FIG. 55.—Gastro-enterostomy for pyloric obstruction. Stoma above the upper limit of the gastric contents in the vertical position. *U*, umbilicus; *P*, peristaltic waves; *S*, stoma. (Hertz.)

*2. Situation of the Stoma above the Upper Level of the Gastric Contents.* In establishing gastro-enterostomy for pyloric stenosis with extreme dilatation of the stomach, it is extremely difficult to judge what point will be the most dependent when the vertical position is assumed. Therefore it was not surprising to find that in one case of dilated stomach due to pyloric obstruction in which no improve-

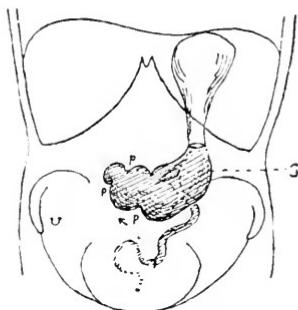


FIG. 56.—Same case as Fig. 55, with abdomen compressed so that the gastric contents can pass out of the stoma. (Hertz.)

ment resulted from operation, the upper limit of the gastric contents did not reach as high as the stoma or the pylorus (Fig. 55). Compressing the lower part of the abdomen caused the contents to rise above the stoma and to pass out of it (Fig. 56). By supplying the patient with an abdominal support and making him recline on his left

side for an hour after meals—the position in which drainage was found to be most rapid—complete relief was eventually obtained. Hertz believes this to be the chief cause for the notorious absence of success of gastro-enterostomy when performed for severe dilatation of the stomach without organic obstruction.

Outland, Skinner, and Clendenning,<sup>1</sup> in a similar study of six posterior gastro-enterostomies, have come practically to the same conclusions.

**PEPTIC ULCER OF THE JEJUNUM FOLLOWING GASTRO-ENTEROSTOMY.** Von Haberer<sup>2</sup> emphasizes the importance of distinguishing between an ulcer directly at the gastro-enterostomy opening and one of the jejunum near by. He mentions having to operate for a too narrow gastrojejunostomy stoma. In the 3 cases of this, the narrowed opening showed absolutely no sign of recent or healed ulcer. He therefore believes it probable that a sufficiently large opening had not been made at the original operation.

According to von Haberer, hyperacidity is a prime etiological factor in the production of jejunal ulcers. According to a number of other operators, the ulcers at the gastro-enterostomy opening, and close to it on the jejunal wall, are the result of trauma from suturing or from pressure of clamps at the time when gastro-enterostomy was performed. For this reason, certain men have discarded clamps, and use other means for avoiding contamination of the operating field. Some elevate the open intestine with stay-sutures to prevent spilling of contents, while others employ simple rubber constriction to accomplish the same purpose.

In the three cases operated upon by von Haberer, the jejunal ulcer was situated on the mesenteric aspect of the gut directly opposite to the stoma, while the stoma itself failed to show any pathological change. In all three cases, other surgeons had performed posterior no-loop gastro-enterostomy; in only one case did this bring relief for about nine months; the others were unimproved.

In his first case, the jejunal ulcer was just on the point of perforating, hence, resection had to be done. The performance of this was very much complicated by the previous gastro-enterostomy with short loop. The entire pyloric region of the stomach was the site of an extensive inflammatory infiltration: this, together with the uppermost loop of the jejunum, was resected. The cut ends of the stomach and duodenum were closed. A Y-anastomosis was made. The lower jejunal end was implanted into the greater curvature of the stomach, and the short jejunal stump of the duodenum was implanted in the side of the jejunum. Three months after operation the patient was reported well.

In the second case, similar conditions were found, with the difference that the pyloric portion of the stomach was not infiltrated and that

<sup>1</sup> *Surgery, Gynecology, and Obstetrics*, vol. xvii, No. 2, p. 175.

<sup>2</sup> *Verhandl. d. Deutsch. Gesellsch. f. Chir.*, 1913.

the jejunal ulcer had penetrated through the wall of the intestine and was densely adherent to the transverse colon and its mesocolon. The affected jejunal loop was resected, also that part of the colon to which it was adherent, together with only as much of the stomach as was immediately adjacent to the stoma. A Y-anastomosis was made as in the previous case. The ends of the colon were blindly closed, and a side-to-side colocolostomy was then done.

In the third case, a button gastro-enterostomy had been made in 1905 for a bleeding ulcer of the pylorus. The opening had contracted. Von Haberer operated for the first time in October, 1911. He found a large, callous ulcer of the pylorus causing marked stenosis. The gastro-enterostomy opening was very narrow, but soft; the jejunal loop was freed from the stomach, and a new no-loop gastro-enterostomy was made. Apparent relief was followed later by recurrence of the old symptoms with bleeding. Von Haberer operated again in February, 1913. The pyloric ulcer was found to be nearly healed; the gastro-enterostomy opening soft and pliable. The jejunal ulcer, as in the other two cases, was located in the mesenteric margin directly opposite the stoma. Transverse resection of that portion of the stomach with which the gut had been joined was done. Pyloric exclusion of the pyloric ulcer followed. The operation was completed as in the previous cases. In spite of the apparent cure, von Haberer feels that in such cases there is a strong tendency to recurrence.

Polya<sup>1</sup> states that 60 per cent. of jejunal ulcers recur after operation.

Clairmont reports 11 cases of peptic ulcer of the jejunum in a series of 368 gastro-enterostomies performed at the clinic of von Eiselsberg, in Vienna. To these are added four operated elsewhere, making a total of fifteen. Of these, 13 cases were in men and 2 in women. In all the jejunal ulcer cases, a posterior no-loop gastro-enterostomy had been done. Only 15 cases of anterior gastro-enterostomy were cited, and none of these had been followed by jejunal ulcers. (It is conceivable that as large a series of anterior gastro-enterostomies might show an equal number of jejunal ulcers.)

In the discussion which followed the reading of Clairmont's paper, Ritter reported a case operated upon by another surgeon six months previously in which he found a large callous ulcer involving the gastro-enterostomy opening, the duodenum close to the pylorus being practically closed. The gastro-enterostomy opening allowed almost nothing to pass. The two limbs of the duodenum were united after the diseased portion had been resected and a new (anterior) gastro-enterostomy established. Six months of temporary relief was followed by recurrence, both in the stomach and jejunum, causing death from inanition.

<sup>1</sup> Zentralbl. für Chir., 1913, p. 544.

Boas, the internist (of Berlin), agreed with von Haberer and Clairmont in that hyperacidity is of the greatest etiological importance in peptic jejunal ulcer.

**Cancer.** SYPHILITIC INVOLVEMENT OF THE STOMACH SIMULATING CANCER. The Wassermann reaction and the  $\alpha$ -ray have shown this disorder to be far more frequent than was formerly supposed. Among recent communications on the subject may be mentioned those of Wolpe<sup>1</sup> and Comite. I also append an  $\alpha$ -ray showing the condition in a patient of Mills<sup>2</sup> (Fig. 57).

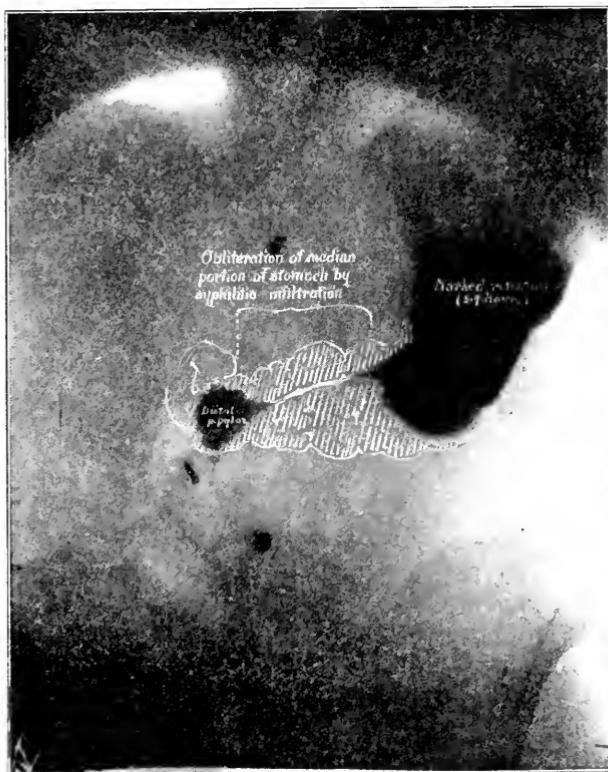


FIG. 57.—Roentgenogram showing obliteration of a large portion of the stomach as a result of massive syphilitic infiltration. Marked obstruction and retention (no evidence of latter in the plate). Complete restoration of stomach shadow occurred after gastrojejunostomy and specific treatment as shown by later examinations. Condition could be easily mistaken for carcinoma. Slightly retouched. (Mills.)

THE ETIOLOGICAL IMPORTANCE OF GASTRIC ULCER IN THE DEVELOPMENT OF GASTRIC CANCER is still the subject of active controversy.

<sup>1</sup> Original in Russian, cit. after Zentralbl. d. gesamte chir. u. i. Grenzgeb., 1913, Band ii, Heft 12, p. 642; Gaz. degli osp., 1913, p. 266

<sup>2</sup> Journal of the American Medical Association, vol. lxi, p. 1347.

On the one hand, we have the ideas of the Mayo Clinic,<sup>1</sup> according to which 71 per cent. of carcinomata of the stomach take origin from the bed of a previous indurated ulcer. On the other hand are those who maintain that these figures are entirely too high. They also adduce clinical and pathological evidence to prove their point. (See Friedenwald, *Boston Medical and Surgical Journal*, May 29, 1913; also the publications of Aschoff, in German.)

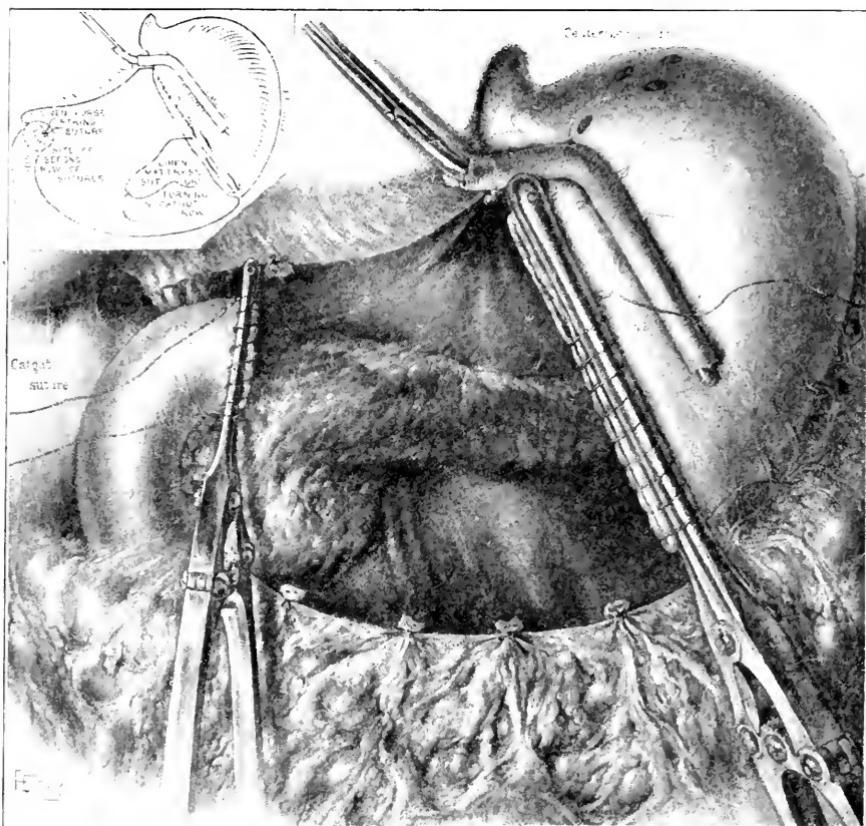


FIG. 58.—Method of closure of the ends of stomach and duodenum by continuous chromic catgut suture, to be followed by musculoperitoneal suture of linen (see small diagram). (Mayo.)

**SURGICAL TECHNIQUE. Technical Points in Performing Resection of the Stomach According to Billroth II.** The method of closing the lumen (stomach, duodenum, and colon) by a running suture over a clamp,<sup>1</sup> the suture being tightened as the clamp is withdrawn, as shown

<sup>1</sup> See papers by Smithies, *Journal of the American Medical Association*, vol. Ixi, p. 1793.

in the accompanying illustrations (Figs. 58 and 59), is giving satisfactory results at the Mayo clinic.<sup>1</sup> Using the same suture, they then carry a running Lembert stitch back to the beginning of the original suture, thus burying the first row of sutures. Perthes<sup>2</sup> also (Fig. 60) expresses his complete satisfaction with this method of Moynihan's.

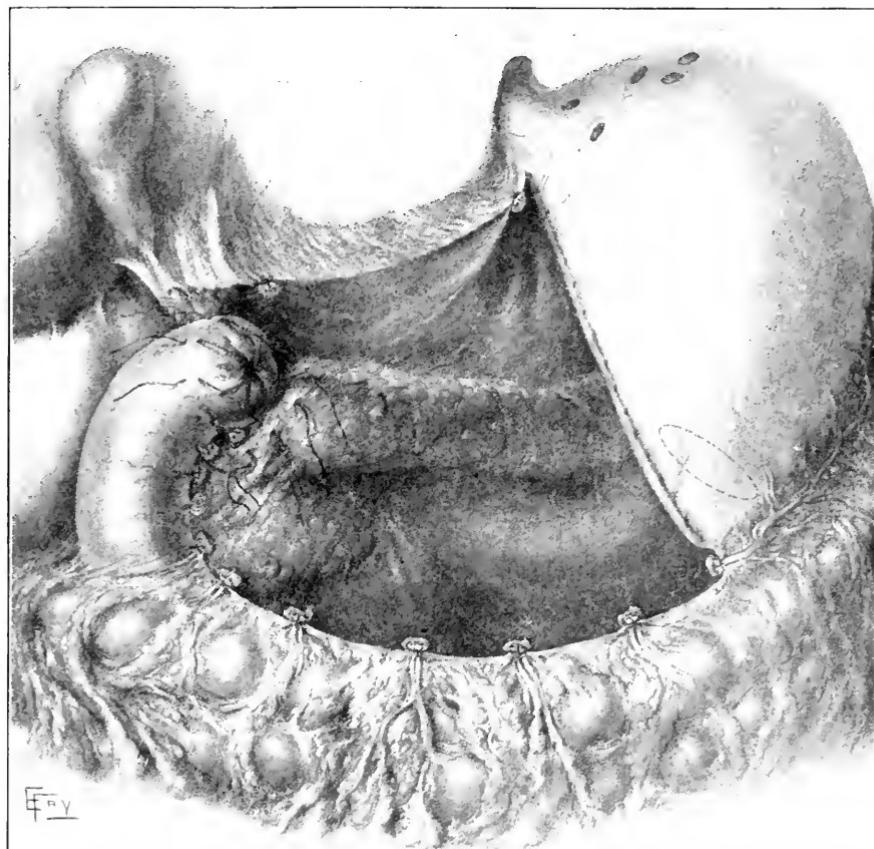


FIG. 59.—Interrupted sutures tying stump of duodenum to pancreas. Dotted line shows posterior gastro-enterostomy. (Mayo.)

Occasionally where the transverse mesocolon is involved in the arcade between the main branches of the middle colic vessels, Mayo says that the involved portion can be removed without endangering the vascular integrity of the intestine. The experiences of Cuneo with injuries of the colic or media artery are in accordance with this (see above). Under similar circumstances, Perthes believes it safer to resect the

<sup>1</sup> Journal of the American Medical Association, vol. lxi, p. 512.

<sup>2</sup> Zentralbl. für Chir., 1913, p. 1097.

middle portion of the transverse colon. He dissents from the advice of Bier first to resect the stomach and affected portion of the transverse mesocolon, then to inspect the transverse colon, resecting whenever its circulation has been interfered with. Instead of this, Perthes recommends resection of the great omentum, transverse colon, mesocolon,

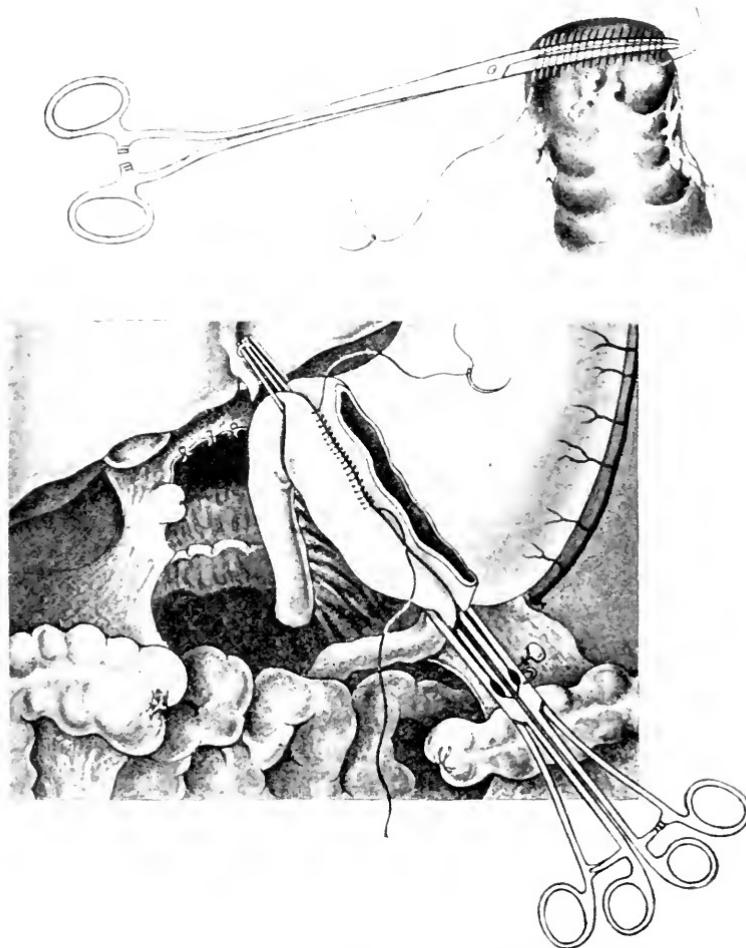


FIG. 60.—Perthes' method of resecting the affected colon and stomach (Billroth II) in one piece.

and stomach in one piece. This gives a much better exposure of the entire operative field and makes for speed, simplicity, and security. Considering the experience of Mayo, Cuneo, and others, the stand taken by Perthes seems to be too radical. However, when the carcinoma

has involved the transverse colon itself, the advantages of his method cannot be gainsaid. As shown in the accompanying illustration (Fig. 60), Perthes employs the Polya-Reichel-Wilms modification of the Billroth II method.<sup>1</sup>

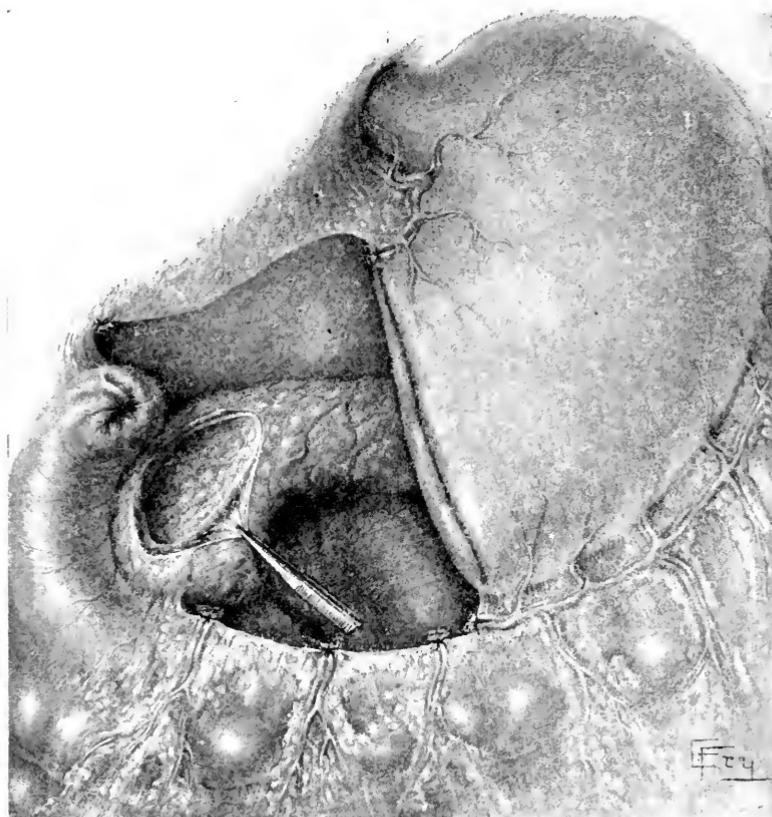


FIG. 61.—Showing excavation in pancreas following resection of pyloric end of stomach with pancreatic involvement. The end of stomach and end of duodenum both closed. (Mayo.)

Finsterer,<sup>2</sup> of Hochenegg's clinic in Vienna, reports a series of thirty-three resections done according to this method, with the difference that the opening in the mesocolon was sutured to the stomach instead of to the loop of jejunum. (Von Haberer in discussing Finsterer's report states that the method was originally evolved by Krönlein and was further developed by Hoffmeister.<sup>3</sup>) After closure of the divided ends, side-to-side colocolostomy is performed.

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1912, p. 93.

<sup>2</sup> Zentralbl. für Chir., 1913, p. 1999.

Ibid., p. 2001.

Moderate involvement of the pancreas does not necessarily preclude radical operation. Mayo states that superficial portions of the pancreas have been satisfactorily removed in over 8 per cent. of his resections.

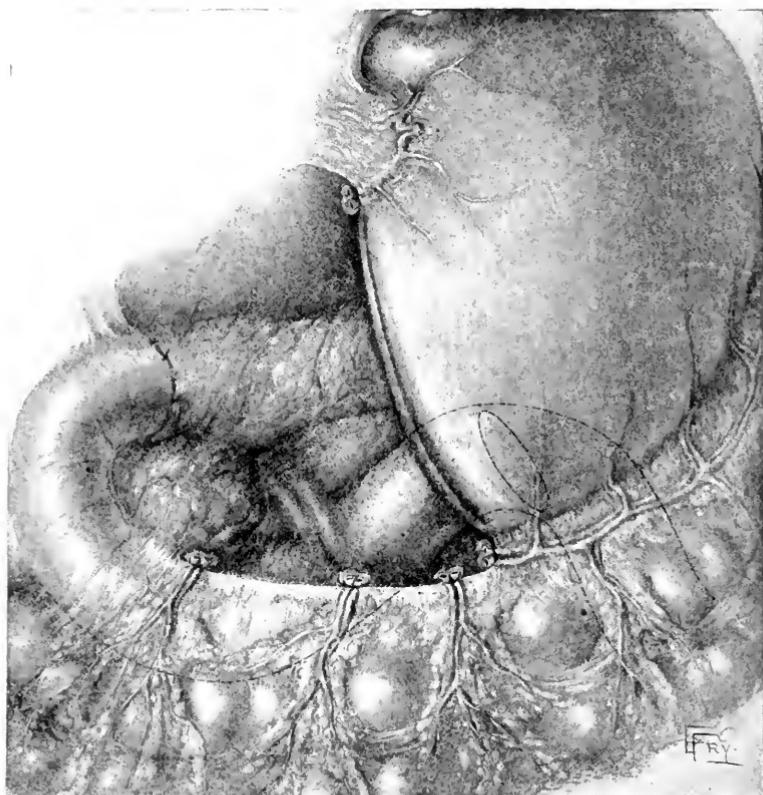


FIG. 62.—Showing operation completed. Closed end of duodenum buried in excavation in pancreas. (Mayo.)

Satisfactory closure of the duodenal stump has always been a matter of concern in performing the Billroth II resection. Smoler<sup>1</sup> reports 8 cases in which he reinforced the duodenal stump by suturing the gall-bladder over it. Four of these patients died in from two to sixteen days after operation. Autopsy showed the duodenal stump to be in good condition. The Mayos use the method of Meyer, closing the end of the duodenum with purse-string sutures (Fig. 61) and implanting it into the excavation made in the pancreas (Fig. 62). Mayo<sup>2</sup> says "we have used this method for something like six years and have not had leakage in a single instance from either the duodenum or pancreas."

<sup>1</sup> Zentralbl. für Chir., 1913, p. 1921.

<sup>2</sup> Annals of Surgery, August, 1913, p. 147.

Of cases where resection for cancer but no excavation of the pancreas has been made, Willy Meyer<sup>1</sup> says: "The adjacent head of the pancreas is then fastened upon the duodenal stump like a cap by means of interrupted sutures. This in turn is covered by a flap of omentum and the abdominal wound is closed without drainage.

*Results.* Mayo<sup>2</sup> reports that, in his clinic, "The mortality in resections is about 10 per cent., depending largely on the quality of cases accepted for operation. With early diagnosis and the patient in good condition, mortality will be less than 5 per cent. There is a prospect of a five-year cure in about 25 per cent., and of a three-year cure in 38 per cent., in the case of those who recover from the operation. Comparatively few patients, who recover following resection, fail to get more than one year of relief."

*Total gastrectomy* was performed by Sasse<sup>3</sup> upon a stomach which had shrunk to a small, tube-like structure; this was isolated along both curvatures and was then divided at the pylorus. The duodenum was closed and buried. Through an opening in the transverse mesocolon, the uppermost jejunal loop was brought upward. The freed stomach was used as a handle to pull down the cardia, to the posterior surface of which the jejunal loop was sutured. The stomach was then ablated, and the intestine was opened and united to the cardia by a circular suture. The patient made a smooth recovery, gaining 26 kilograms within a short time.

The specimen failed to show any evidence of cancer; callous ulceration had led to an enormous thickening of the wall (2 cm.).

At no time had the patient vomited blood or had there been blood in the stools. Since operation (a year and a half), there has been no complaint except a lack of satiety after eating.

Max Cohn<sup>4</sup> reported the *x-ray* examination of a woman whose entire stomach had been removed for cancer in July, 1912, by Unger. The food at first distended the esophagus to the level of the diaphragm, but stayed there. Ingestion of more material resulted in dilatation of the lower end of the esophagus, and a thin stream of food could be seen passing vertically down into the small intestine, where its passage was very much delayed. Cohn attributes this diverticulum formation of the lower esophagus and the slowing of the peristalsis in the small intestine to the fact that both vagus nerves had been resected at the time of operation. There was marked anemia in spite of the well-nourished condition of the patient.

<sup>1</sup> Zentralbl. für Chir., 1914, p. 54.

<sup>2</sup> Journal of the American Medical Association, vol. lxi, p. 542.

<sup>3</sup> Münch. med. Woch., 1913, No. 12.

<sup>4</sup> Berlin. klin. Woch., 1913, No. 30.

### THE DUODENUM.

**Duodenal Diverticula and Duplicatures of the Duodenal Wall.** According to Wilkie,<sup>1</sup> duodenal diverticula are not as rare as their occurrence in the literature might lead one to believe. He accounts for this impression by the ease with which the condition may escape notice at a post-mortem examination unless one is on the lookout for it. Sixty-eight cases occur in the literature, 83 per cent. of which were in patients over fifty years old. The majority of diverticula occur in the second part of the duodenum. They are usually single, although there are instances where four or five diverticula have been found in the same individual. At times, symmetrical diverticula lie to either side of the common bile duct. In the majority of cases they show no secondary pathologic changes and have nothing to do with the death of the patient. However Bauer and Wilkie each had 2 cases of duodenal diverticulum with pathologic changes in adjacent organs. In one case of Bauer's, a mass of soft accumulated material in the diverticulum led to compression of the duodenum. In the other case, the diverticulum was filled with a foul semifluid mass of material; there was a duodenal catarrh, with swelling of the papilla of vater and ieterus. In Wilkie's 2 cases, the diverticulum and the common bile duct lay alongside of one another, and in both cases there was stasis in the choledochus.

Diverticula in the second and third part of the duodenum are of congenital origin. Besides congenital diverticula in the first part of the duodenum, there are also those arising secondary to ulcer and having a wide opening into the vestibulum duodeni. Congenital duplicatures of the duodenal wall occur by themselves or together with diverticula. In all probability they represent persistence of anatomic conditions which regularly occur at certain stages in fetal development. The duplicatures represent a moderate degree of the same congenital anomaly which, in its most extreme form, leads to a congenital atresia of the duodenum.

**The Diagnosis of Conditions in the Duodenum by Means of the X-ray** is of more recent development than that of the stomach or colon. The normal duodenum empties itself with great rapidity, hence it is not easy to obtain pictures of this organ filled with bismuth. David<sup>2</sup> introduces an Einhorn's duodenal tube into the duodenum, brings the patient in front of the Röntgen screen, and then floods the duodenum with 100 c.c. of bismuth carbonate in water. Carman<sup>3</sup> states that at the beginning of a screen examination before the bismuth meal is taken, a little plain water and bismuth facilitates palpitory outlining of the

<sup>1</sup> Edinburgh Medical Journal, 1913, p. 219.

<sup>2</sup> Zentralbl. f. inn. Med., 1913, No. 21, p. 521.

<sup>3</sup> Journal of the American Medical Association, August 2, 1913, p. 321.

borders of the stomach, and, by not exciting the pyloric reflex, can ordinarily be expressed into the cap and duodenum, thus visualizing it.

The superior horizontal portion of the duodenum, the bulbus duodeni, or "cap," ordinarily shows as a small cone with its base directed downward and separated from the stomach by the pyloric ring (Fig. 63). This first portion of the duodenum has a smooth inner wall and shows a regular outline when filled with bismuth. The second and third portions show the inward section of the valvulae conniventes. In cases in which the cap or first portion of the duodenum is vertically above the pylorus, bismuth tends to collect here by means of gravity and is sometimes seen in a thin, disk-like layer above the pyloric region; this is in "fish-hook" stomachs. In "steer-horn" stomachs the cap



FIG. 63.—Normal adult stomach. *x-ray* after bismuth meal. Note that the duodenal cap and pyloric part of the stomach are to the right of the spine. (*x-ray* by Dodd.)

is often in the horizontal axis of the stomach and no disk-like residue accumulates. Like the stomach, the first portion of the duodenum may be distorted by ulcer. The well-known signs of perforating ulcer hold for this part of the duodenum as they do for the stomach. Strands of adhesions from the gall-bladder may produce irregularities (see *x-ray Diagnosis of Cholecystitis*). Stenosis is shown by dilatation and delay of contents above it as elsewhere in the alimentary tract. A tender pressure point on the duodenum is not necessarily pathognomonic of ulcer, and therefore its importance should not be overestimated.

Cole,<sup>1</sup> the first one to use the term pyloric cap, makes the following remarks about variations which resemble pathological deformities

<sup>1</sup> Journal of the American Medical Association, vol. lxi, p. 752.

seen in some of the plates of every series. He says that these can be readily recognized and definitely differentiated from organic changes. "The small indentations frequently observed on either the left or right side of the cap may be due to pressure from the descending portion of the duodenum, the common bile duct, or the vena portae. Spasmodic contraction of the cap (Fig. 64) is often the result of iliac stasis, a Lane's kink, or a diseased appendix (contrast this with Lane's statement). Incomplete filling of the cap may be caused by overactive duodenal peristalsis. This is more likely to occur in the early stage of digestion when the pyloric sphincter is strongly contracted, than in the later stages when the sphincter is relaxed and the gastric peristalsis is more efficient, even though less active. The function of the cap is that of a reservoir. During the early stage of digestion, the contents are rapidly withdrawn from the reservoir cap, but, as digestion progresses, the cap is more completely filled with the acid chyme.

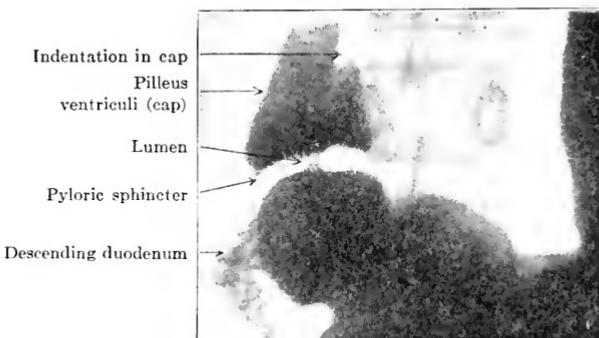


FIG. 64.—*Pilleus ventriculi* (cap). (Cole.)

The cap is separated from the pars pylorica by a space varying from one-eighth to one-quarter of an inch, indicating the pyloric sphincter (Figs. 63 and 64). The importance of the pyloric sphincter's Röntgenographic appearance is second only to that of the cap in diagnosis of this region. Both its gastric and duodenal surfaces should be smooth and clear-cut, and the lumen should be centrally located. The degree to which the pyloric sphincter is contracted is in direct proportion to the activity of the gastric peristalsis."

Carman states that the following symptoms may appear when duodenal ulcer is present:

1. Early free opening of the pylorus, with early clearance of the stomach.
2. Lagging of bismuth in the duodenum.
3. Residue in the stomach (sometimes in the duodenum) after six hours, if there is an obstruction from scar contraction.

4. Pressure tender point over the duodenum.
5. Dilatation of the cap.
6. Irregular outline of the cap or duodenum.
7. Diverticulum of perforating ulcer.
8. Vigorous peristalsis, especially if there is obstruction.

It is of the utmost importance to bear Carman's warning in mind, namely, that radiological diagnosis of duodenal ulcer, unless corroborated by clinical data, is, in most instances, a mere guess. Excluding obstructive cases, the Röntgen-ray appearance of duodenal ulcer is often seen when the actual lesion is elsewhere, as in the appendix or gall-bladder.

The report of Altschul<sup>1</sup> bears out this statement. Seven cases, with the typical *x*-ray picture of duodenal ulcer, failed to show any lesions of the duodenum at operation. Two cases proved to be carcinoma of the cardiac end of the stomach; two appendicitis; two mechanical patency of the pylorus (whatever that may be), and one tuberculosis of the ileum and cecum. All the patients were women.

George and Gerber<sup>2</sup> state that the lateral illumination, as employed by Cole, has been of great use in diagnosing and demonstrating duodenal ulcer. W. H. Stewart has his patients lie on the right side.

**Duodenal Ulcer. THE PATHOLOGY OF DUODENAL ULCER.** W. J. Mayo<sup>3</sup> calls attention to the fact that a considerable percentage of ulcers of the anterior wall of the duodenum have different characteristics from those of the stomach, characteristics which have been the cause of much confusion because they fail to conform to the standard of gastric ulcers. Thus a typical gastric ulcer is a punched-out defect in the mucous membrane, with a sclerosed, grayish-white base surrounded by a thickened margin of overhanging mucosa. In contrast to this, certain ulcers on the anterior wall of the duodenum with obstruction and callus, upon excision often show a defect scarcely larger than a dimple. This defect may resemble a little slit in the mucosa; sometimes it is surrounded by an area of thickened, congested mucous membrane like a patch in the duodenum. In several instances, having a well-marked callus, the ulcer could scarcely be detected, although the changed spot of mucosa directly underneath the callus was quite evident. Apparently there is no relation on the one hand between the size of the callus in the submucous, muscular, and peritoneal coats and the amount of obstruction, and, on the other, to the actual size of the ulcer, which varies from a mere slit to the size of a pea. Even in larger ulcers of the anterior wall, the base is not clear-cut and grayish white like a gastric ulcer, but resembles a moth-eaten patch.

In other cases, ulcers of the gastric type are found on the anterior

<sup>1</sup> Zentralbl. f. Chir., 1913, No. 52, p. 2000.

<sup>2</sup> American Quarterly of Röntgenology, 1913, No. 4, p. 187.

<sup>3</sup> Annals of Surgery, May, 1913, p. 691.

wall of the duodenum. These have a raised, corn-like elevation on the peritoneal surface corresponding to the base of the ulcer. Opposite to them on the posterior wall, may be a contact ulcer of the eroded mucous type.

Ulcers of the posterior duodenal wall present the same characteristics as those of the stomach. There is a clean-cut, definitely punched-out area closely attached to the pancreas and usually completely perforating the duodenal wall. A callus which forms the base of the ulcer prevents perforation. In such cases as in callous ulcer of the anterior wall, there is a contact ulcer opposite (in this case on the anterior wall), just across from the lesion on the posterior wall.

These pathologic findings demonstrate why this type of ulcer might be overlooked, and probably has been overlooked, in average routine examination of the duodenum at autopsy. These findings also explain why the diagnosis of chronic ulcer of the duodenum may not furnish demonstration by the *x-ray*.

**SURGICAL TREATMENT OF DUODENAL ULCER.** Ulcers of the anterior wall of the duodenum may be excised in suitable cases with satisfactory result without performing gastro-enterostomy (the thick, calloused, obstructive duodenal ulcers are not suitable for excision). The excision of the ulcer should be accompanied by division of the pyloric sphincter using either the Finney or the Heinecke-Mikulicz method of pyloroplasty for closure. The gastroduodenal opening should be made at least two and one-half inches long. The Mayos have excised 52 chronic duodenal ulcers without performing gastro-enterostomy and report excellent immediate and late results. Excision should be limited to duodenal ulcers of the anterior wall.

Excision of four posterior ulcers of the duodenum proved to be so difficult, as contrasted with gastro-enterostomy, that the Mayos are not inclined to continue the practice, although the four patients recovered and have all remained well.

The callous contracted ulcers with obstruction are ideal cases for gastro-enterostomy. Infolding sutures of silk or linen are applied in such a manner that the entrance to the duodenum is obstructed; this prevents food from entering the ulcerated portion. As a rule, the Mayos place an obstructing suture just above the pylorus for this purpose. They state this method of producing obstruction, although temporary, will last long enough to enable healing to take place, and ulcers so treated will recur but rarely. If recurrence does take place, it will be necessary to make the obstruction permanent, either by complete division of the pyloric end of the stomach and turning both sides in—the method of von Eiselsberg—or, more easily but less surely, by drawing a piece of fascia obtained from the sheath of the rectus muscle close about the stomach just above the pylorus and suturing it in such position as to obstruct the lumen, as recommended by Wilms (see Pyloric Exclusion below).

A number of patients upon whom gastro-enterostomy with infolding of the duodenal ulcer was performed over fifteen years ago have remained in excellent health.

**Pyloric Exclusion.** Unilateral pyloric exclusion was first brought into prominence by von Eiselsberg.<sup>1</sup> Briefly, this consisted in dividing the stomach completely across and closing both ends blindly, after which a gastro-enterostomy was performed with the oral sac. Almost everyone agrees that the end-results of this operation in cases of pyloric or duodenal ulcer are most satisfactory. The only objection, and this is a very important one, is the added time necessary to complete the operation, which is, of course, accompanied by a somewhat higher mortality than simple gastro-enterostomy.

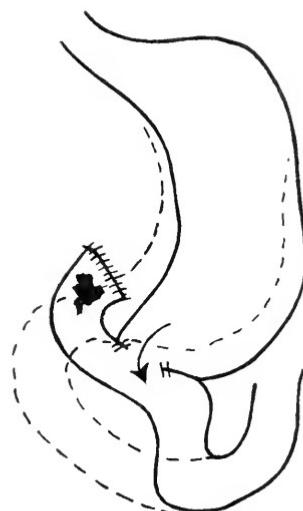


FIG. 65.—Brun's method of partial pyloric exclusion.

A whole host of methods have been tried for excluding the pylorus in a speedier, simpler manner. These may be divided as follows:

#### I. Variations of Suture Method.

Dobbertin<sup>2</sup> divides the stomach transversely, as in the typical Eiselsberg operation; closes the duodenal stump blindly; through an opening in the transverse mesocolon he draws up the first jejunal loop as close as possible to its beginning and unites this to the open end of the stomach as described in PROGRESSIVE MEDICINE for June, 1912, p. 94. This saves one row of sutures in the original operation.

Brun<sup>3</sup> also divides the stomach in the pyloric portion transversely, closes the duodenal end blindly and implants the stump of the stoma into the side of the second portion of the duodenum (Fig. 65).

<sup>1</sup> Von Eiselsberg's unilateral pyloric exclusion was reviewed in PROGRESSIVE MEDICINE, 1911, p. 112.

<sup>2</sup> Zentralbl. für Chir., 1914, p. 1441.

<sup>3</sup> Ibid., p. 140.

Rossi<sup>1</sup> uses an instrument similar to that devised by Hürtl<sup>2</sup> for gastric resection. Two parallel rows of metal sutures are simultaneously inserted by simply pressing down a lever of the machine. The stomach is cut across between the metal suture lines, and each is buried beneath a Lembert stitch.

## II. Simple Constriction of the Pyloric End of the Stomach.

For simple constriction of the pylorus, Parlavecchio originally employed a cord. Many of those following along the same line have used finer ligature material; this has cut through. Thus Borszky,<sup>3</sup> of Réeczy's clinic at the University of Budapest, quotes a series of 20 cases in which silk ligature was used. Three of these were examined by the x-ray four to five months later, and showed patency of the pylorus. This was confirmed at operation; it was barely possible to recognize the site of ligation. The temporary closure was supposed to have aided in the healing of the ulcer. Parlavecchio himself now advocates a woollen band 1 cm. wide, the ends of which should be sewed together—not knotted. This is buried under a serous suture or by an omental flap. An occlusion lasting a few months is all that he claims for this method.

Fascial strips were first used by Wilms. He reported 18 cases at the meeting of the Deutsche Gesellschaft für Chirurgie in 1913. x-ray showed the pylorus to be closed. The case reported by Bier, of Berlin, in which at a second laparotomy many perigastric adhesions were found around the fascial strip, led Hoffmann<sup>4</sup> to devise a method for avoiding this complication. He remarks, "If the fascial strip is buried by joining the intact stomach wall over it, there is a tendency for the Lembert stitches to cut through on account of the constant pull by the peristaltic movements of the stomach walls, and so the fascial strip is again exposed." To avoid this, Hoffmann suggests dividing the serosa and muscularis<sup>5</sup> and applying the constricting fascial strip to the exposed mucosa, over which the divided tissues are united, thus burying the strip. If anything, peristalsis now assists in occlusion instead of opposing it.

The ligamentum teres has been employed in 7 cases by Polya.<sup>6</sup> It is dissected free, passed around the stomach and partially knotted, and then fixed in position by suture. Two of Polya's patients died within three weeks after operation. At autopsy, it was found that occlusion was not complete, the opening just admitting a small probe.

Bircher<sup>7</sup> frees the umbilical end of the round ligament of the liver,

<sup>1</sup> Osp. magg. Milano, vol. i, p. 233.

<sup>2</sup> See PROGRESSIVE MEDICINE, 1912, p. 62.

<sup>3</sup> Zentralbl. für Chir., 1913, p. 569.

<sup>4</sup> Ibid., p. 1331.

<sup>5</sup> It is not essential to divide the serosa and muscularis on the posterior aspect of the stomach if there is the least difficulty.

<sup>6</sup> Zentralbl. für Chir., 1913, p. 1329.

<sup>7</sup> Ibid., p. 1547.

passes it once or twice around the pylorus, and fastens it to itself by suture.

A strip of sheet aluminium 1 cm. wide and about 5 cm. long drawn through behind the stomach, then rolled snugly around the pylorus with the fingers, makes sufficient compression to obliterate the lumen. In experiments on dogs, Brewer<sup>1</sup> found that while this occluded the pylorus it did not affect the vitality of the tissues. In every one of nine dogs, there was mechanical closure of the pylorus, and in animals living longer than nine days the band was invisible, being completely embedded in newly formed tissue. There was no macroscopic or microscopic necrosis of the compressed tissue present.

In all the articles dealing with constriction of the pylorus, great stress is laid on preserving a nice balance between sufficient tension to occlude the pylorus and not enough to constrict the tissues (in order to avoid a cutting through of the ligature). It would seem as though such exact adjustment could most easily be made by the method of Brewer.

### III. *Pyloric Exclusion plus Suspension.*

Hoffmann<sup>2</sup> observed ptosis of the stomach after gastro-enterostomy with development of a vicious circle. After ligature of the pylorus with a fascial strip, he fastened its free ends to the abdominal wall.

Hercher<sup>3</sup> also noted the development of gastrophtosis after gastro-enterostomy. He, too, used a fascial strip for constricting the pylorus and suspending it, the ends of the strip being pulled through the peritoneum and muscle, and sutured to the external aponeurosis apparently in the same fashion as the round ligaments of the uterus are fastened to the aponeurosis in Gilliam's operation.

Goebell<sup>4</sup> accomplished the same result by means of a much more complicated operation. In two cases of gastrophtosis with marked dilatation, a strip of the rectus sheath was used to ligate and suspend the pylorus. A longitudinal seromuscular flap with its base near the pylorus was fashioned from the anterior wall of the stomach; it was used to surround the fascial suspensory ligament. The sides of the defect of the stomach wall were then united, narrowing its lumen. It is to be noted that the employment of interrupted stitches thus unnecessarily delays the completion of this rather complicated operation.

Mariani<sup>5</sup> is the most radical. After performing gastro-enterostomy and while closing the abdominal wound, he sutures the kinked pylorus to the rectus in the laparotomy wound just below the free border of the ribs, thus suspending and occluding it.

Pagenstecher<sup>6</sup> reports recurrence of gastrophtosis within three

<sup>1</sup> Surgery, Gynecology, and Obstetrics, 1914, p. 145.

<sup>2</sup> Zentralbl. für Chir., 1913, p. 1169.

<sup>3</sup> Ibid., p. 1707.

<sup>4</sup> Ibid., p. 1332.

<sup>5</sup> Ibid., p. 1706.

<sup>6</sup> Münch. med. Woch., 1913, No. 1.

months after suspension by means of fascial strips according to the method of Wilms. He advocates gastropexy by means of the ligamentum teres of the liver. This structure is freed from the umbilicus after ligation of the artery running in it. The lower part of the suspensory ligament of the liver, of which the ligamentum teres is the free border, is dissected free from the anterior abdominal wall. This flap is reflected backward and to the left, against the anterior wall of the stomach, to which it is sutured. Röntgen examination one and a half years after operation revealed the pyloric part of the stomach raised upward toward the right without materially affecting its form or motility.

**HEMORRHAGE FROM DUODENAL ULCER.** Thompson<sup>1</sup> reports 2 cases of fatal hemorrhage occurring within forty-eight hours after gastro-enterostomy for duodenal ulcer. In discussing the treatment, he says, "it is proved beyond doubt that in the majority of cases of duodenal ulcers associated with hemorrhage, gastro-enterostomy will check the bleeding. This is shown conclusively in Moynihan's series of cases of severe hemorrhage, 18 in number, where the operation was unattended by any mortality."

It would seem more reasonable to believe that the hemorrhage stopped of itself irrespective of whether or not gastro-enterostomy was done. He quotes Moynihan's recommendations for either ligating the artery just before it enters the ulcerating mass or massive infolding of the duodenal wall over the ulcer. No mention is made of Rovsing's gastroduodenoscopy (reviewed in PROGRESSIVE MEDICINE for June, 1911, p. 106) or of the recommendation of Wilms to introduce the finger through a small opening in the stomach and palpate the interior of the duodenum.

**PERFORATION OF GASTRODUODENAL ULCERS.** *Symptoms.* In a masterly description of the symptoms of perforated ulcer, Deaver<sup>2</sup> says, "The leading symptom is pain; the leading sign is rigidity; the leading clue is a history of previous indigestion of ulcer type. The pain and the rigidity are invariably present. The suggestive history is occasionally lacking." After giving details of these various points he says, "This is a practical picture of perforated ulcer. If it is remembered and all the rest forgotten, I am convinced that more diagnoses will be made than are made at present." And again, "The attempt to place any other symptom or sign on the same plane of importance with those just mentioned will, in individual cases, result in disaster."

The relative value he places on the *subsidiary symptoms and signs* are so just, that I quote them in part: "Shock at the onset has been observed. In a greater or less degree it is not infrequently associated with the severe pain of perforation. But people are differently con-

<sup>1</sup> Annals of Surgery, May, 1913, p. 694.

<sup>2</sup> Journal of the American Medical Association, vol. lxi, p. 75.

stituted in respect to the reaction to pain. Shock may be slight or very transient, and in most patients after a very few hours not even the slightest element of shock can be seen.

Vomiting is almost constant and is a symptom of value. It is not invariably present, however, and is a symptom of such common occurrence in varied general and abdominal disorders that it serves but little purpose in diagnosticating the condition of perforation. Nausea and vomiting may be noted as of almost uniform association of auxiliary, but not distinctive value. Blood in the vomitus is seldom seen, but when present, is decidedly helpful.

The temperature, pulse, and respiration rates are very misleading if the attempt is made to attach diagnostic importance to them. A few of the observations made on the operative cases in his series are cited:

| Temperature. | Pulse. | Respiration. |
|--------------|--------|--------------|
| 98.3         | 104    | 24           |
| 99.4         | 92     | 24           |
| 99.0         | 108    | 34           |
| 97.4         | 112    | 32           |
| 98.2         | 78     | 36           |
| 99.0         | 96     | 28           |

These observations are fairly illustrative of the temperature, pulse and respiration, at times ranging from six to fifteen hours after perforation. It will be seen that the temperature is least affected, not infrequently being normal, but naturally showing a slight tendency toward elevation.

The pulse is, as a rule, moderately accelerated. Again, it may be normal. There is nothing distinctive in its quality, which is frequently full and good.

The respirations are, as a rule, slightly increased. This is due, more than to any other factor, to the rigidity of the abdominal muscles and the diaphragm, which forces the breathing to assume the true costal type, necessitating more frequent respirations for the purpose of aeration. In short, in the remedial stage of perforation, there is nothing in the temperature, pulse, or respiration to suggest the urgency of the patient's condition. Later, when the patient is getting ready for the pathologist instead of the surgeon, the temperature, pulse, and respiration show great changes, a description of which is interesting for the student of the biology of disease but lacking in help to the sufferer.

Distention, the accumulation of fluid in the abdomen, and the subsidence of peristalsis, "the silent belly," are also terminal events, of prognostic, but not of diagnostic, importance.

Free gas in the abdominal cavity and the obliteration of liver dulness are also signs which should be stricken out of the text-books or labelled indelibly as false friends. Too much stress has been laid on these signs

as indicative of perforation of the bowel. Liver dulness may be diminished or abolished either by gas in the peritoneal cavity or by gas in the intestine, but, in either case, it requires a large amount of gas to produce this effect. If the gas is in the intestine, it requires marked distention, which, in the case of perforated ulcer, can come about only when peritonitis is advanced and, as a rule, irremediable. If it be free gas in the peritoneal cavity which causes obliteration of liver dulness, it must be present in considerable amount.

As an aid in helpful diagnosis, therefore, the obliteration of liver dulness is more of a hindrance than a help.

The leukocyte count is of some help, chiefly in differentiating such non-inflammatory conditions as gastric crises and abdominal angina. In the majority of cases, a leukocytosis appears very quickly. On the other hand, in a well-marked, diffuse peritonitis eight and one-half hours after perforation, the leukocyte count was 7300 and the polymuclear percentage was 70. Deaver remarks, "I deprecate the attempts which are occasionally made to set up the leukocyte or polynuclear count as arbiters of diagnosis or of prognosis."

*Tenderness in the pouch of Douglas as an early sign of perforation* is spoken of by Kulenkampff.<sup>1</sup> A man, aged twenty years, with a perforated ulcer of the lesser curvature, showed, within three hours after perforation, exquisite tenderness in the pouch of Douglas. At operation stick sponges were passed into either flank and into the pelvis without bringing up any exudate. The fact that the acid gastric secretions are particularly irritating to the sensitive parietal peritoneum has been brought out by Mayo, in discussing Deaver's paper, and is also mentioned by Kulenkampff.

*Treatment.* As a matter of course, immediate laparotomy is the only thing to do. There is decided lack of unity among various authorities regarding the treatment of the ulcer opening as well as the indications for a gastro-enterostomy under these conditions.

Deaver reports a series of 26 patients operated upon for perforation. Of these, eight had gastric and eighteen duodenal ulcers. One died. In only two of the gastric ulcer cases was there simple suture of the ulcer; the remaining six had a gastro-jejunostomy in addition. Whenever the patient's condition permitted, the following line of treatment was carried out: (1) Closure of the ulcer. (2) Plication of the duodenum to obliterate its lumen and fortification of this area by covering with the gastrohepatie and gastroeolic omentum. (Deaver purposely causes pyloric stenosis by plication in order not only to safeguard the closure of the perforation but to establish and render permanent the function of the new opening.) (3) Posterior no-loop gastrojejunostomy. (4) Tube drainage of the pelvis through a suprapubic stab.

<sup>1</sup> Deutsch. med. Woeh., 1913, vol. 39, 110.

In the discussion following Deaver's paper, W. J. Mayo stated that among a number of different plans for treating a perforated gastric ulcer within the first twelve hours, one of the best was to draw up the stomach, put a drain into the opening (see Neumann's omental cuff below, and drain also the bottom of the peritoneal cavity).

Babcock reported 18 cases of acute perforated ulcers of the duodenum, in none of which gastro-enterostomy was performed. Of these 18, 16 patients were men. Three of the 18 died. The rest recovered. Babcock's treatment consists in putting a pad against the ulcer, draining the abdomen, and putting the patient to bed. Of these fifteen patients, fourteen remained free. In the only one continuing to show ulcer symptoms, a secondary gastro-enterostomy was performed. In the case of the others, Babcock pointed out that if a gastro-enterostomy had been done, the good result would have been ascribed to this, rather than to simple drainage of the abdomen, drainage of the ulcer region, and plugging of the ulcer with gauze.

In England, Corner<sup>1</sup> took a similar but less extreme stand than Babcock. He reported a series of 40 cases of perforated gastroduodenal ulcer; 33 per cent. were entirely cured; 67 per cent. were only partially cured. He opposed primary gastro-enterostomy and favored a secondary one three to six months after the first operation, giving the following reasons: In about 50 per cent. of the cases, a gastro-enterostomy is unnecessary because the ulcer is situated in the cardiac half of the stomach, and of the patients with ulcers in the pyloric part of the stomach quite a number have recovered without any further operation than simple infolding of the ulcer. Gastro-enterostomy is of value only when there is stenosis of the pylorus.

In Germany, Seidel<sup>2</sup> reports 14 out of a series of 19 cases with simple infolding of the ulcer by a special method of stitching (see below) which has given satisfactory results. He is now making a series of infoldings plus gastro-enterostomy merely for the sake of comparing the two methods of procedure.

The protection afforded by gastro-enterostomy against subsequent complications of ulcer, either hemorrhage or perforation, is relative, not absolute. Hemorrhage has been treated elsewhere. Leeene,<sup>3</sup> in reporting a series of five perforations from gastroduodenal ulcer, mentions perforation from an ulcer in the anterior wall of the stomach two years after a posterior gastro-enterostomy.

The collective report on 200 cases of perforated duodenal ulcers published in the *Edinburgh Medical Journal*, 1913, does not add anything very new to the subject.

<sup>1</sup> Proceedings of the Royal Society of Medicine, vol. vi, No. 5, Surgical Section, p. 164.

<sup>2</sup> Zentralbl. für Chir., 1913, p. 1481.

<sup>3</sup> Press. méd., 1912, No. 86.

*A reinforced suture for closure of perforation opening in friable tissue* is described by Seidel.<sup>1</sup> In applying this stitch he advises the operator to bear the following principles in mind. (1) The stitches should be applied well away from the opening of the perforation. With small ulcers it is possible to include the entire callous area in the stitches and thereby invert it. With very large ulcers, only the majority of the infiltrated tissue can thus be treated. (2) The first row of sutures should be of heavy silk and should perforate the entire thickness of the stomach wall. (3) Either a row of Lembert sutures which reach to non-infiltrated tissue or else a flap of omentum should reinforce the through-and-through sutures. The details of technique are as follows:

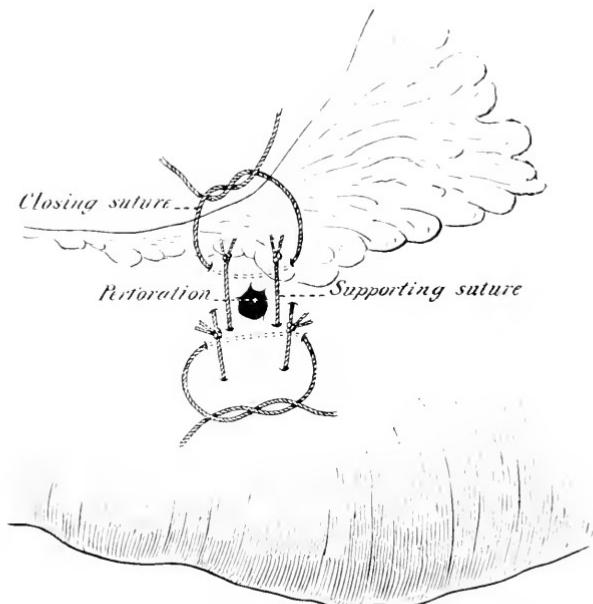


FIG. 66.—Seidel's reinforced suture for closing perforations.

To either side of the perforation opening at a distance of about 1 cm., heavy through-and-through silk sutures are placed parallel to one another and perpendicular to the greater and lesser curvatures. These are tied just tight enough so as not to cut through the friable callous tissue. At right angles to these (Fig. 66) interrupted sutures which also perforate all walls of the stomach are passed, which, if not too tightly knotted, are furnished an excellent support by the first line of sutures. Another row of Lembert sutures, or a flap of omentum, reinforcing the closure. This has proved to be extremely solid (in experiments on dogs and cadavers). Similar principles of suture have been

<sup>1</sup> Zentralbl. für Chir., 1913, p. 1481.

used by Payr for hemostasis in liver tissue, by Hagner for uniting tendons, and by Perthes for closing transverse abdominal incisions.

Oehlecker<sup>1</sup> reports excellent results in closing perforated ulcers by the method of Seidel.

*Neumann's Omental Cuff.* The method was first published four years ago. A drainage tube is introduced through the perforation opening of a gastric or duodenal ulcer so that its end lies well down in the duodenum. That part of the tube lying between the perforation and the anterior abdominal wall is surrounded by a cuff of omentum. A circular suture fastens this cuff to the wall of the stomach or duodenum immediately adjacent to the perforation opening. A longitudinal suture joins the two omental surfaces to form a tube from the perforation opening to the anterior abdominal wall. A second circular suture then approximates the end of the omental cuff to the margin of the abdominal wound. The first nourishment is introduced through the drain within six to twenty-four hours after operation. In the meantime, large amounts of fluid have escaped by the drain. Up to the fifth day, all nourishment is given through the tube, then it is supplemented by a carefully selected fluid diet until the eleventh day. After removal of the tube (anywhere between the twelfth and seventeenth day), the opening closes rapidly. Neumann<sup>2</sup> employed his method in 13 cases of perforated gastroduodenal ulcer; 11 of these were duodenal, 1 prepyloric and 1 high up near the cardia. Seven patients recovered and six died, the latter all came to operation more than eighteen hours after perforation. Neumann considers his method suitable for draining any part of the intra-abdominal alimentary tract. He has used it in six gastrostomies. He claims that after it the stomach's peristaltic movements cannot drag upon the parietal peritoneum of the anterior abdominal wall, thereby causing subjective distress, as in other methods of gastrostomy.

In this connection it may be worth while to remark that for some years past a similar principle has been observed in performing cholecystostomy. The gall-bladder is no longer fixed to the parietal peritoneum, but is allowed to drop back into its normal position. No leakage occurs. There are no adhesion pains.

## THE SMALL INTESTINE.

**Intestinal Obstruction.** Some excellent experimental work done in this country at the Johns Hopkins and the Cornell Medical Schools has recently been published.

<sup>1</sup> Zentralbl. für Chir., 1914.

<sup>2</sup> Deutsch. med. Woch., 1913, Band xxxix, p. 554.

Whipple, Stone, and Bernheim<sup>1</sup> in a series of ninety dogs operated upon in the Hunterian Laboratory of the Johns Hopkins Medical School, ascertained the following facts: After isolating the duodenum from below the pancreas to its entrance into the jejunum, and establishing a posterior gastro-enterostomy, they found that the dogs died with the symptoms of volvulus or of a high ileus. If the isolated, closed loops were thoroughly washed out at operation, the animals lived somewhat longer, rarely more than three days. Enormous amounts of fluid were lost through vomiting and diarrhea. There was a small pulse, low blood pressure and elevation of temperature. Normal dogs, injected with the toxic contents of the isolated loop, died with similar symptoms. Drainage of the isolated loop permitted the animals to live for months. Whipple, Stone, and Bernheim come to the conclusion that a poisonous substance is found in the closed duodenal loop, which is absorbed, causing intoxication and death. Further experiments<sup>2</sup> along the same lines led to the following conclusions: The mucous membrane of the closed or drained duodenal loop contains a toxic substance which is identical with the toxic material found in the lumen of the closed loop. This toxic substance is formed by the mucous membrane itself and is absorbed by it.

Normal duodenal mucous membrane contains no toxic substance, nor is it able *in vitro* to neutralize this toxic substance generated by the mucous membrane of the closed duodenal loop, nor will the normal mucous membrane absorb this toxic substance. Destruction of the mucous membrane in the blind loop hinders production of the toxic substance.

In Hartwell's<sup>3</sup> experiment upon intestinal obstruction, great care was taken not to injure the tissues or impair their circulation. An accurately adjustable clamp was applied with just enough pressure to obliterate the lumen, but not sufficient to impair the circulation of the compressed tissue. The most important fact brought out by him was that if the water, lost by vomiting or by diarrhea, is replaced by subcutaneous saline solution, the dog may be kept alive for as long as three weeks without apparent distress.

Wilkie<sup>4</sup> does not agree with the conclusions of Stone, Bernheim, and Whipple, his reasoning, however, is not convincing. He confirmed the work of Hartwell and Hoguet in prolonging the lives of animals by administration of fluid subcutaneously. The most important point brought out in the rest of the paper was confirmation of the findings of Murphy and Vincent, that obstruction of the venous return was the most important factor in producing an early fatal result, and that an isolated loop of intestine survived ligature of both arteries and veins

<sup>1</sup> Journal of Experimental Medicine, 1913, xvii, p. 286.

<sup>2</sup> Ibid., 1913, pp. 307 to 323.

<sup>3</sup> Ibid., August, 1913.

<sup>4</sup> British Medical Journal, October 25, 1913, p. 1064.

for a considerably longer time than ligature of its veins alone. Aside from this, very little new was added to the knowledge of the subject.

In one of his conclusions, Wilkie stated that "peritonitis plays no part in causing death in the majority of cases of simple intestinal obstruction; in cases of strangulation, however, it may undoubtedly be a factor in the later stages." Howell,<sup>1</sup> in controverting this point, maintained that the peritoneal cavity was the seat of the absorption of toxins. "In health, organisms penetrate through the intestinal walls into the peritoneal cavity, a trap specially designed to receive and annihilate them, with its own excretory apparatus, the liver and intestines, so arranged that their poisonous excretions are not admitted into the systemic vessels. In disease, such as intestinal obstruction, the number and virulence of the organisms in the afferent intestine are increased enormously, permeation of these into the peritoneal cavity is excessive, and throws an increased strain upon the peritoneal excretory machinery, as evidenced by the copious vomiting, fatty degeneration of the liver cells, dryness of the tissues, and so forth." The fact that the presence of bacteria in the peritoneal cavity has not been proved by experimental bacteriologists under such conditions is ascribed to improper technique by Howell. In a later letter to the *British Medical Journal* (page 1646), Howell backs up his argument by quoting the statement from Dudgeon and Sargent regarding the extreme ease with which bacteria pass through the bowel walls in pathological conditions even in the early stages of intestinal obstruction. Howell goes on to say, "my theory is that the seat of the production of the toxin and of its absorption, is the peritoneal cavity in cases of acute intestinal obstruction. Mr. Wilkie and others have proved most conclusively that it is not the lumen of the alimentary canal; but this puts Mr. Wilkie in a difficulty, for since the bowel is the only source of toxin which suggests itself to his mind, and his own experiments have put this out of court, he is forced to conclude that splanchnic paresis with depletion of the systemic circulation, is the main factor in producing the symptom-complex of acute intestinal obstruction, and that this paresis is first produced reflexly by intestinal distention so that a vicious circle is set up which can be broken through, in cases of simple obstruction, by enterostomy.

"I have shown in my first letter<sup>2</sup> that this symptom-complex can be broken through by draining the peritoneum in such cases *without enterostomy*, and, if that is not sufficient, take the case of a strangulated ovarian cyst which gives rise to the same symptom-complex as acute strangulated bowel, yet this symptom-complex can be made to disappear by removal of the cyst even though the pedicle continues to be strangulated by a thick ligature. If the symptom-complex were purely a nerve reflex set going by a non-toxic stimulus, such as the strangling of nerve fibers and vessels in the pedicle, there is no reason why the mere removal of

<sup>1</sup> British Medical Journal, November 15, 1913, p. 1333.

<sup>2</sup> Loc. cit.

the cyst should cause it to disappear; but if we consider the symptom-complex to be evidence that the excretory apparatus of the peritoneum is attempting to get rid of toxins from its interior, then our results are easily explained, for a strangulated ovarian cyst is an infected cyst from which infection pours out into the peritoneal cavity, and, by removing the poison factory, we remove the stimulus which reflexly sets the peritoneal excretory machinery in motion." A discussion of the other less important points in the Howell-Wilkie controversy, most of which have been settled some time ago, would take up too much space.

**Resistance of the Myenteric Nerves to Anemia.** Cannon and Burkett<sup>1</sup> find that if vessels supplying parts of the alimentary canal are ligated, the tissues become edematous and purple but may not be completely anemic. Even if this condition has persisted for six or seven hours, such regions may recover normal activity upon resumption of circulation, histological examination showing nerve cells normal in appearance. Complete anemia from compression may last as long as three hours and yet be followed by a return of former motility. Compression anemia for three hours and one-half or longer, invariably causes loss of function and disappearance of nerve cells in the compressed parts. In short, the presence or absence of function depends upon the continued existence or destruction of the myenteric plexus of nerves. Their resistance to anemia for so long a time, shows them thus far to be the most hardy nerve cells found in the body.

**Gas Cysts of the Intestines.** A clear summary of the existing views regarding this rare and curious affliction is given by Turnure,<sup>2</sup> who publishes a case of his own and summaries forty-nine others collected from the literature. Practically all the reported cases with accurate clinical histories and autopsy protocols in detail, showed either the presence of gastric or duodenal ulcers, or symptoms indicating the existence of some chronic disease of the intestinal tract for a number of years previously.

The cysts may occupy any layer of the intestinal wall. They are known to have disappeared within a few weeks after simple laparotomy.

Turnure's patient was a Chinaman, aged fifty-seven years, who had a perforated gastric ulcer. At laparotomy, one and a half gallons of serosanguineous clear fluid were removed from the peritoneal cavity by aspirator (Pool's aspirating tip). Lying in the right lower quadrant of the abdomen were several loops of the small intestine matted together and covered by hundreds of small cysts, many of them pedunculated and containing gas. The cysts promptly collapsed upon puncture. The perforation in the stomach was stopped with a piece of omentum upon which a cigarette drain was firmly placed. The patient died eight hours after operation.

<sup>1</sup> American Journal of Physiology, 1913, p. 347.

<sup>2</sup> Annals of Surgery, June, 1913, p. 811.

The following excerpts from the autopsy are of interest: "In the right lower quadrant of the abdomen, a dozen or more coils of the small intestine were bound together by serofibrinous exudate, forming a large, convoluted, sausage-like mass, and in the peritoneal covering are dozens of pale, tense bullæ which collapsed on section, with the escape of air. The smallest of these blebs approximated the size of a split pea, while the largest was about the size of a crab-apple, and each was covered externally by peritoneum (Fig. 67). Upon exposing the mucous surface of the gut corresponding to the distribution of the gaseous



FIG. 67.—Macroscopic appearance of a gas cyst of the intestine. (Turnure.)

bullæ, large numbers of pinhead-sized emphysematous vesicles were found irregularly scattered beneath the epithelial lining; otherwise the mucous membrane showed no noteworthy macroscopic changes. Large and small emphysematous blebs were also observed dispersed through the peritoneum in front of both kidneys."

The cysts could be traced for a short distance into the mesentery; here their structure was the same as in the mucosa. At the margins of the lesion there was a gradual transition between the large cysts and the normal intestine, the cysts dwindling down to microscopic size. Summary of the pathologic findings:

1. Extensive gas-cyst formation, for the most part situated outside of the longitudinal muscular coat.
2. Characteristic appearance of the gas cysts and the cyst walls, in which the presence of an endothelial-like lining and giant cells is a feature.
3. Occurrence of spaces or channels, some of which may be lymphatics partly lined by endothelium and partly filled with giant cells, endothelioid cells, and leukocytes.
4. Evidences of dilatation of lymphatics and of the intercommunication of large lymphatic spaces, possible cyst spaces, with undoubtedly lymph channels.
5. Absence of communication between cysts.
6. Inflammatory and productive processes between the cysts and under the peritoneum, resulting in the formation of connective tissue and fibromatous masses, leading to the obliteration of certain cysts and therefore to a kind of healing process.
7. Absence of bacteria in most of the cysts. (The bacteria present in some places are probably postmortem invaders.)
8. The disposition of highly refractive needles in the interior of many of the cysts, causing a peculiar flattening of the cells belonging to the lining membrane, and the possible role of such crystalline matter, in the production of some of the giant cells.

After a brief historical survey, Turnure outlines the four existing theories in regard to the cause of this condition. These are:

1. *A Bacterial Theory*, endorsed by the majority of authors in which formation of the cysts is ascribed to the action of gas-producing organisms.
2. *A Mechanical Theory*, according to which intestinal gas escapes from minute ruptures in the bowel wall, thus leading to cyst formation.
3. *A Neoplastic Theory*, whose adherents believe there is "a distinct variety of tumor, the cells of which have the faculty of secreting gas" (Finney).
4. *A Chemical Theory*, which may be described as a combination of the neoplastic and mechanical theories.

There is no treatment, since several secondary laparotomies have shown that the cysts disappear of their own accord.

Resection of the intestine, puncture and evacuation of the cysts, or ligation of pedunculated ones, as recommended by Mjassiniikoff,<sup>1</sup> are entirely unnecessary.

Since the appearance of Turnure's paper an additional case was reported by Thalheimer.<sup>2</sup> Here, too, there was a perforated gastric ulcer in addition to the cysts of the small intestine. Microscopic examination revealed a similar condition to that reported by Symmers,

<sup>1</sup> Original in Russian, cit. after Zentralbl. f. d. gesamte Chir., 1913, Band i, p. 597.

<sup>2</sup> Proceedings of the New York Pathological Society, 1913, p. 5.

who examined Turnure's specimens. The cysts were almost entirely lined with endothelium. There were cubical, cylindrical, and giant cells; the latter occurred not only in the wall of the cysts but also in the adjacent connective tissue and in the lymph spaces and capillaries. Thalheimer believed the blocking of the lymph vessels by endothelial proliferation might be of significance in the causation of the cysts.

### THE APPENDIX.

**The Leukocyte Count in Acute Appendicitis.** Among the most important points brought out in Deaver's masterly book on *Appendicitis*<sup>1</sup> are the statements that the leukocyte examination affords no indication of the type of local process present, and, that the polymorphonuclear count should be abandoned as a guide in establishing an operative indication. He makes the same points in his article on Duodenal Perforation (see p. 124 of this article). The more one sees of acute abdominal conditions, the more heartily does one concur with Deaver's views.

**The Subserous Appendix, Should it Be Isolated or Removed?** This has been the subject of a grave controversy running through the *Zentralblatt für Chirurgie*<sup>2</sup> of 1913. The article of Kofmann<sup>3</sup> was the starting-point of this controversy. A boy of fourteen was operated a few days after an acute attack of appendicitis had subsided. The appendix was so buried in adhesions that it could not be freed. The base, close to the cecum was the only accessible portion. Here the appendix was divided, the cecal stump was invaginated and closed with a diagonal stitch (rediscovered by Sultan); about 1 cm. of the friable appendix was resected, and a purse-string suture was put around the protruding stump, which was invaginated and then covered with a bit of omentum. Because his patient made an uneventful recovery, Kofmann advises employment of this "isolation" of the appendix in similar cases.

This exhumation of a long-settled question did not of itself deserve notice (nor did it receive any last year when I first read it), but the many communications to which it gave rise, it requires a brief comment. In fairness it must be said, that all subsequent communications on this question disagree with Kofmann. Instructive cases are cited to prove that the appendix, if left behind, is bound to cause subsequent trouble. The subserous shelling out of the appendix is also discovered anew. In short, questions between ten and twenty years old are discussed as though they had been raised for the first time. Long ago in this country the lesson was learned that simple drainage of an appendix abscess tided the patient over for the time being, but

<sup>1</sup> *Appendicitis*, fourth edition, P. Blakiston's Son & Co., 1913.

<sup>2</sup> *Zentralbl. f. Chir.*, pp. 85, 87, 271, 423, 506, 680, 1068, and 1364.

<sup>3</sup> *Ibid.*, 1912, p. 1700.

that if the appendix was left behind, sooner or later it was sure to cause trouble again. The subserous shelling out of the appendix is accurately described both in Kelly's book (1905) and in Sprengel's<sup>1</sup> monumental monograph.

**Counter-drainage in the Loin of Retrocecal Appendicular Abscesses** is recommended by Jackson.<sup>2</sup> This is rarely done nowadays. However, there will always be certain cases in which it is indicated.

**The Treatment of Suppurative Pylephlebitis after Appendicitis.** The communications of Wilms and Sprengel were reviewed in PROGRESSIVE MEDICINE, June, 1911, p. 135; their recommendations consisted in exposure and ligation of the venous radicles near the ileocecal angle. During the past year Braun<sup>3</sup> has improved upon this procedure. In his report, suppurative pylephlebitis of appendicular origin occurred 8 times in a series of 600 cases of appendicitis. Four of these cases ran a typical course. There were chills, enlargement of the liver, icterus, followed by death within a short time after the onset. At autopsy, the ileocolic vein was found filled with suppurating thrombi. In two instances these were in open communication with the appendicular abscess. The thrombosis continued up into the root of the superior mesentery vein and into the portal vein. There were multiple suppurative foci throughout the liver. In all 4 cases, the main trunk of the ileocolic vein was the only pathway by which the septic thrombi could have reached the portal vein. Had the ileocolic vein been ligated at its junction with the superior mesenteric vein Braun states, it might have been possible to save the lives of these four patients. According to him the ligation or resection of the main trunk of the ileocolic vein is not difficult. He opens the abdomen with the patient in slight Trendelenburg position. A transverse incision, made a little higher than the anterior-superior spine, nicks the rectus near the linea alba. After packing off the general peritoneal cavity, the appendix and its adjacent abscess are first attended to. Then under good exposure the cecum and ascending colon are drawn over to the right, the small intestine to the left, and the transverse colon upward. Now the posterior parietal peritoneum (ascending mesocolon) is exposed from the ileocecal angle to the vertebral column. The main branch of the ileocecal vein running upward and inward lies directly beneath the peritoneum. In thin persons it may be seen beneath the peritoneal covering, and when thrombosed may be felt as a hard, cord-like structure. The overlying peritoneum is split, the main trunk of the vein is exposed, and is followed upward to the vertebral column, where it is ligated as close as possible to its junction with the superior mesenteric vein.

<sup>1</sup> Appendicitis, Billroth-Luecke, Deutsch. Chir. Published in 1906.

<sup>2</sup> Journal of the American Medical Association, vol. ix, p. 1285.

<sup>3</sup> Beitr. z. klin. Chir., Band lxxxvi, Heft 2.

As early as 1907, Braun attempted this operation on a patient who subsequently died. More recently, he has had two successful cases. In one, the main trunk of the vein was not thrombosed, and the patient recovered without further complications. In the other, 8 cm. of the vein plugged with suppurating thrombi, were resected, and two abscesses in the mesocolon communicating with the diseased vein, were opened and drained. In this case the chills ceased immediately. The jaundice and enlargement of the liver gradually subsided. It took a long time for the abscesses in the mesocolon to heal.

In comparing his ligation of the vein close to its junction with the superior mesenteric vein, to that of Wilms, where the radicles of the vein close to the gut are ligated, Braun intimates that the latter procedure is more likely to be followed by disturbances of circulation than his own. He expressly states that not the slightest disturbance in circulation followed ligation of the main trunk of the ileocecal vein. Naturally, the earlier this operation is done, the better is the chance of its localizing the source of infection.

**Local Anesthesia in Appendectomy for Chronic Appendicitis.** Fowelin<sup>1</sup> cites 54 cases in which the following technique was carried out: By means of suitable infiltration, the abdominal wall and the peritoneum are anesthetized between points *A* and *B* (Fig. 68). To render the parietal peritoneum anesthetic from *B* to *E*, that is, from the anterior spine down to the cecum, the needle is first introduced in the direction of the arrow *C* until it strikes against the bone. It is then withdrawn a little, and, always preceded by preliminary injection, is gradually passed down parallel to the flare of the ileum but 1½ to 2 cm. away from it in the direction of arrow *D* to a depth of 6.7 cm. The needle is now withdrawn and from the same superficial opening, is again plunged parallel to the ileum but about 45 degrees upward, then in a similar way downward (the first direction which is directly backward). Twenty c.c. of a 1 per cent. novocain-adrenalin solution are injected; then twenty to twenty-five minutes are allowed to elapse before operation is begun. The onset of anesthesia may be hastened by gentle massage of the infiltrated region. The only pain felt by the patients was when the mesenterolum of the appendix was ligated. The pains were always referred to the stomach. In 6 cases of subacute appendicitis with adhesions, small amounts of a general anesthetic were needed in addition to the local anesthesia. The method is not suitable for acute cases.

**Chronic Appendicitis.** Codman,<sup>2</sup> of Boston, agrees with the pathologists who state there is no evidence of any real condition of chronic inflammation in a so-called chronic appendix, and who consider the surgical chronic appendices as healed or healing appendices following

<sup>1</sup> Zentralbl. für Chir., 1913, p. 342.

<sup>2</sup> Boston Medical and Surgical Journal, October 2, 1913, p. 495.

acute attacks. Codman quotes Aschoff's view, namely, that the demonstration of obliteration proves a previous inflammation, and incidentally that over 50 per cent. of autopsy examinations show a previous inflammation according to this criterion. The following convincing figures are adduced to show *the impossibility of accurately diagnosing lesions of the appendix in the absence of acute attacks.* Out of 100 abdominal sections taken at random from the Massachusetts General Hospital

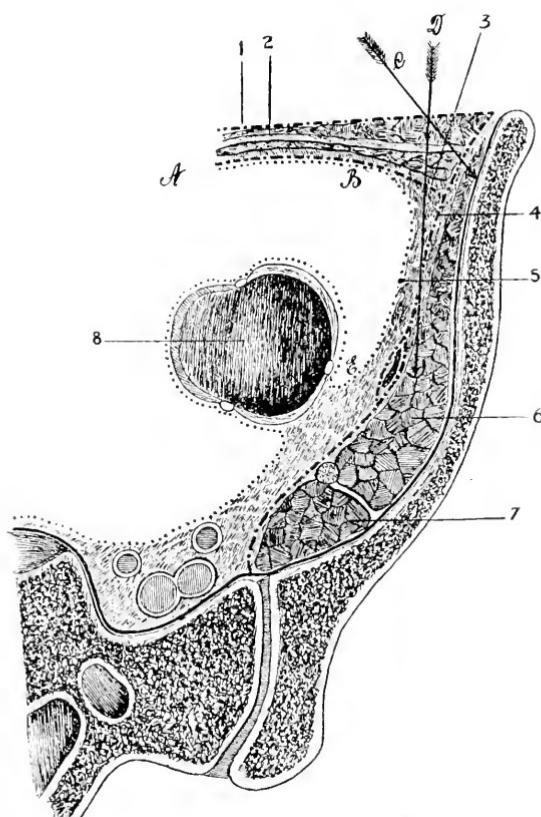


FIG. 68.—Fowelin's method for local anesthesia of the parietal peritoneum; the arrows indicate the direction of the needle. 1, aponeurosis of external abdominal muscle; 2, internal abdominal muscle; 3, transverse fascia; 4, iliac fascia; 5, parietal peritoneum; 6, iliac muscle; 7, psoas major muscle; 8, cecum.

records, 71 showed definite lesions of the appendix, although no such preoperative diagnosis was made from the history. On the other hand, in a series of 98 cases operated by Codman and diagnosed definitely as chronic appendicitis, only 61 showed pathologic evidence. Definite peritoneal adhesions, stricture, and obliteration have only been considered as pathologic evidence. Mere thickenings have been barred out.

In 17 of Codman's 98 cases, one of the following conditions was found to be the real cause of symptoms; chronic salpingitis, tuberculous mesenteric gland, inguinal hernia, gall-stones, ovarian cyst, pelvic kidney, tapeworm, cardiospasm, megasigmoid, ptosis and mega-duodenum, appendix abscess, and syphilis. But 6 of these 17 also had a chronic appendix. Constipation was rarely associated with chronic appendicitis.

Bastedo's test, consisting in inflation of the colon with air and thus exaggerating local pain and tenderness, was unreliable. It was positive 12 times when it should have been negative, and was present only 14 times in the 61 definitely diseased appendices.

In critically reviewing his series of 98 cases, Codman states that while 61 showed evidence of having been inflamed, 50 of these should have been excluded because they had definite histories of classical acute attacks. Codman emphasizes that tenderness at McBurney's point for a day or two after the pain has disappeared is of the utmost importance in diagnosing an acute attack of appendicular inflammation.

Regarding the *x*-ray diagnosis of appendicular disease, Codman agrees with foreign observers that our available knowledge is not sufficiently extensive to furnish much positive evidence.

**The X-ray Diagnostics of the Appendix.** Gourcerol<sup>1</sup> employs the following method for diagnosing conditions in the right iliac fossa. Six to eight hours after a bismuth meal has been given, metal markers are put upon the umbilicus, the anterior-superior spine, and the point of maximum tenderness; a wire is used to designate the outer margin of the rectus. With the patient lying flat upon the back, palpation is controlled by means of the fluoroscope. It is important to determine whether the ileocecal angle corresponds to the point of greatest tenderness. The mobility and the relationship of the cecum, appendix, and terminal ileum, can be determined. In spite of all this, the information gained is not adequate to furnish operative indications, nor does it tell us whether or not the appendix is diseased.

The experience of Max Cohn,<sup>2</sup> of Berlin, is similar to that of Gourcerol. Examination is begun four hours after the bismuth meal has been taken. As in the *x*-ray examination of other parts of the alimentary canal, it is of the utmost importance to make a *series* of examinations at different times and to compare all these before coming to any definite conclusions, so as to avoid mistaking physiologic processes for pathologic conditions.

It was found that the appendix became filled with bismuth mixture whenever its lumen freely communicated with that of the cecum. The position of the appendix changed with the posture of its owner. The appendix followed the peristaltic movements of the cecum and was

<sup>1</sup> Med. Prat., 1913, No. 44, p. 689.

<sup>2</sup> Deutsch. gesellsch. für Chir., 1913, also Deutsch. med. Woch., 1913, p. 606.

found to move of its own accord around the cecum, the latter naturally being the fixed point. As a rule, bismuth entered the appendix some time after the cecum had become filled. This varied from seven to eight hours after the bismuth meal had been taken, to as late as the day following, in contrast with the filling of the cecum, which regularly occurred within four hours after ingestion. According to Cohn, the antiperistaltic movements of the cecum filled the appendix, while its own peristaltic movement emptied it. The appendix has been seen to fill and empty a number of times during the digestion of one meal. There may be delay in the emptying of the appendix so that bismuth is present in its lumen long after the cecum has become empty. Peristaltic movements of the appendix have been observed to give rise to temporary constrictions similar to the haustral segmentation of the cecum. These are physiologic, and should not be interpreted as stenoses or partial obliterations.

Fränkel,<sup>1</sup> in discussing the paper of Cohn, with which he agreed, laid great stress upon the necessity of repeated examinations extending over a number of days. He reported having followed individual cases as long as eleven, and even twenty-nine, days. He united with Cohn in emphasizing that, at present, our knowledge is too fragmentary to enable us to draw definite conclusions from the *x-ray* pictures. Nevertheless, he believes it fairly safe to state that an appendix which is quickly filled with bismuth and which completely empties itself within one or two days, may be looked upon as healthy.

Cohn, in closing, stated that only after a great many comparisons have been made between the *x-ray* pictures and the findings at operation, will we be able to separate normal from pathologic pictures.

**Appendicostomy Instead of Jejunostomy** is recommended by Spisharny<sup>2</sup> in cases in which the stomach requires an absolute rest for a time and hence artificial feeding must be resorted to. It seems worth trying.

**Dermoid Cyst of the Meso-appendix.** This rarity was removed from a man, aged forty-three years, by Willems.<sup>3</sup> Eight years previously, after the acute symptoms of an appendicular attack had subsided, a tumor was palpable. This remained unchanged until the subsequent operation. The tumor which was found lying between the leaves of the meso-appendix was extirpated. It proved to be a dermoid cyst.

Another pathologic curiosity is the *black (pigmented) appendix*, 4 cases of which are reported by Battle.<sup>4</sup>

Microscopic examination showed that the pigment lay in the mucous membrane, both in and between the cells. Chemical analysis demonstrated this pigment to be some form of iron, the exact combination of which could not be made out on account of the small quantity available.

<sup>1</sup> Zentralbl. für Chir., 1913, p. 515.

<sup>2</sup> Ibid., p. 1217.

<sup>3</sup> Beitr. z. Klin. Chir., 1913, Band lxxxvi, Heft 1, p. 223.

<sup>4</sup> Laneet, July 19, 1913.

**THE LARGE INTESTINE.**

**Intestinal Stasis.** The writings of Lane and his followers have been very fully reviewed in previous numbers of this article.<sup>1</sup> During the past year they<sup>2</sup> reiterate the same theories and reasoning.

In the article by M. F. Fallon,<sup>3</sup> is the observation made by Lane that red-headed people are not subject to Jackson's membranes. Fallon also says that Lane believes 90 per cent. of cases with stasis are curable by medical means, and in only 10 per cent. are surgical measures indicated. One would never suspect this moderation from reading the other papers published on the surgery of intestinal stasis and its indications.

During the past twelve months, three important communications, each from the pen of an authority in his own branch of medicine, have appeared, controverting the theories of Lane.

W. Hale White<sup>4</sup> criticises the expression "alimentary toxemia," stating that the group of men who use this phrase cannot identify the bacterial organisms which are the source of this condition nor have they made any scientific dissection of the various steps in the process.

That intestinal stasis is the cause of alimentary toxemia is by no means proved. Certain individuals may bear fecal impaction of five or six weeks' standing with apparent unconcern, as in the case published by Harris,<sup>5</sup> of a man, aged sixty-two years, with fecal impaction lasting forty-nine days, and, a year later, lasting fifty-three days, without bad results.

In my article last year I expressed the doubt<sup>6</sup> whether all possible medical means had been employed in cases of so-called intestinal stasis before resorting to the knife. I am glad to see that so eminent an internist as Hale White holds a similar view. He says: "When these cases are reported, we are always assured that all medical means have been adopted without benefit, but we are never told what the medical means were. . . . The suspicion comes to one's mind sometimes that, perhaps some of the surgeons do not know all the means the physician has at his command for the treatment of delayed action of the

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1911, p. 122; June, 1912, p. 106; June, 1913, pp. 114 to 148.

<sup>2</sup> Lane, W. A., Surgery, Gynecology, and Obstetrics, 1913, vol. xvi, No. 6, p. 600; also British Medical Journal, November 1, 1913; Jordan, A. C., Practitioner, 1913, vol. xc, No. 2, p. 441; Schlesinger, Boston Medical and Surgical Journal, July 3, 1913, p. 14; Pringle, Gray, and Chaple in British Medical Journal, January 17 and 24, 1914.

<sup>3</sup> Boston Medical and Surgical Journal, October 23, 1913, p. 600.

<sup>4</sup> Proceedings of the Royal Society of Medicine, 1913, vol. vi, Supplement, Part 1.

<sup>5</sup> Journal of the American Medical Association, vol. lx, p. 722.

<sup>6</sup> PROGRESSIVE MEDICINE, June, 1913, p. 114.

bowels." I would go even farther than this and state that, with certain striking exceptions, little or nothing is known about scientific dietary control of the intestinal functions in this country, by the majority of either surgeons or internists. Nor is this to be wondered at, considering the low general level of cooking in this country—in fact, one might say that our cooking is still in the kettle and fry-pan state.

Hertz,<sup>1</sup> the Röntgenologist, controverts many of the statements made by the school of Lane, saying that the so-called pathognomonic signs of intestinal stasis, *viz.*, the loss of flesh, pigmentation of the skin, pungent sweat, cold hands and feet, headache, lassitude, and abdominal discomfort, may indicate such a variety of conditions that they might even be adduced to prove the exact contrary. Hertz examined a number of such cases of constipation. The *x*-rays showed that the intestine brought its contents through to the large gut within normal time limits. The cause of constipation lay in the fact that the people themselves had become so accustomed to depend upon cathartics to move their bowels, that they no longer felt any desire for stool except with such artificial aid. Like all other scientific Röntgenologists, Hertz emphasizes the necessity of making a long series of plates extending over considerable periods of time in order to diagnose chronic constipation and to identify the particular segment of the intestinal canal responsible for it. From his extensive experience, Hertz makes the following statements:

Intestinal stasis never leads to delay in emptying the stomach and never causes kinks, widenings, or ulcer formation in the duodenum. On the contrary, duodenal ulcer is usually associated with an exaggerated motility of the stomach and small intestine. The so-called iliac stasis is a physiologic condition, caused by the activity of the ileocecal sphincter. This can be increased either through spasm of the muscle or through its insufficiency as a result of disease in the neighborhood of the cecum. The fact that loops of the intestine hang down into the pelvis is never the cause of stasis, with the exception of very rare cases, where such dropping of the transverse colon may cause a stenosis at the splenic flexure. The presence of the cecum or the transverse colon, in the true pelvis, is entirely compatible with complete health. In most cases of constipation, one single region of the large intestine is responsible for the condition.

White and George<sup>2</sup> hold the same general views. "Stenoses at the duodenojejunal angle are not very rare. They may produce much dilatation of the whole duodenum and greatly delay the passage of bismuth. In our experience, kinking at the jejunal angle, is rather rarely found with ulcer, and it seems unlikely that these ulcers are largely

<sup>1</sup> British Medical Journal, 1913, April 19.

<sup>2</sup> Boston Medical and Surgical Journal, July 31, 1913, p. 157.

secondary to such kinks and the resulting stasis and absorption, as Jordan and others<sup>1</sup> have stated."

One fails to note in the communications of the Lane school any clear-cut separation of cases into the various well-known forms of constipation as revealed by serial x-ray study—for example, those of Stierlin,<sup>2</sup> who divides obstipation into the following forms:

1. *Dyschezia.* In which the stool reaches the sigmoid flexure within the customary time. Here it remains for days, and some of it is even visible after a movement of the bowels has taken place.

2. The *constipation of the "ascendens" type*, in which the intestinal contents lingers for an unusually long time in the beginning of the large intestine.

3. The *obstipation* associated with the ptosis of the transverse colon, in which the feces remain in the ptotic transverse colon for a longer time because of diminution, or even absence, of the large peristaltic movements. (See also "PROGRESSIVE MEDICINE, June, 1913, pp. 127 to 132.")

According to Adami,<sup>3</sup> the word "auto-intoxication" ought to be banished from the vocabulary of all self-respecting medical men. He says, in part, "While the symptoms and diseases enumerated by Sir Arbuthnot Lane may follow intestinal stasis, at least a large proportion of these may originate independently of such stasis." Adami recommends that before advising the operation of short-circuiting, it is necessary to make the fullest studies in order to discover, if possible, the nature of the organisms responsible for the disturbance and its probable seats of entry. He believes that discovery of the cause of symptoms will suggest appropriate means of treatment other than short-circuiting, and only when these have been tried and found wanting, will removal or short-circuiting of the colon be justifiable. He points out the grave and eminent danger that immature surgeons of two continents, encouraged to regard the colon as a common sink and therefore of no account, will inaugurate an era of short-circuiting, performing this and colectomy for all sorts of conditions on the slightest possible pretext.

Jackson,<sup>4</sup> speaking of Lane's surgical treatment of intestinal stasis says: "His first efforts were directed, however, to a simple short-circuiting by ileocolostomy. From this he derived much benefit, but not complete satisfaction. The well-known fact of reverse peristalsis in the colon would still carry contents back into the segment which he desired to exclude. He then began the plan of supplementing the ileo-sigmoidostomy by excision of greater or less segments of the remaining

<sup>1</sup> See article by Schlesinger, a pupil of Lane's, in the Boston Medical and Surgical Journal, July 3, 1913, p. 14.

<sup>2</sup> Ergebnisse d. inn. Med. u. Kinderheilk., 1913, Band x, p. 383.

<sup>3</sup> British Medical Journal, January 17 to 24, 1914.

<sup>4</sup> Annals of Surgery, March, 1913, p. 395.

colon, and, a few years ago, advocated the radical excision of the entire colon from the ileocecal junction to the sigmoid. This radical suggestion met with little acceptance elsewhere, on account of its apparent magnitude. And now Mr. Lane, himself, has abandoned the plan because of several instances of distressing after-effects and an excessive mortality, mainly from true adhesion. In his latest communication, he has returned to the simple ileosigmoidostomy, now supplementing it, however, by an effort to establish a new and artificial kink above his point of anastomosis, to prevent a reverse peristalsis carrying the feces back to the right colon. This method has not long been used, and his ultimate experience with it is as yet conjectural." (See also the remarks below on ileosigmoidostomy.)

**Jackson's Membrane, Pericolonic Membrane.** Briefly summarized, our present knowledge about these structures consists in the following facts: Membranes are found in 15 per cent. of fetuses. The same approximate figures hold for autopsies upon children. In adults they have been found upon the right side (*pericolitis dextra*, Binnie) and upon the left side (*pericolitis sinistra*, Eastman). Probably these fetal structures<sup>1</sup> never cause trouble unless they become the seat of a low-grade productive inflammation.

The case of Bevan<sup>2</sup> would indicate that pericolic membrane may also develop during adult life, independent of any fetal condition. He removed the appendix in a case showing no sign of pericolic membrane. A year later he reoperated and found a well-developed membranous pericolitis.

In the course of his impartial summary of the subject, Jabez Jackson,<sup>3</sup> says, "Our personal observation of a now considerable number of cases at operation (35 cases) rather inclines us to the belief that perhaps varied causes may be responsible for the production of this pericolonic membrane. We have one case previously reported, in which the membrane (in this case involving the entire cecum as well) was undoubtedly the sequence of an antecedent acute peritonitis of appendicular origin. This case had been one of walled-in appendicular abscess with drainage without removal of the appendix. At the time of our later operation all the walling-in adhesions were gone, but the vascular membrane was well marked. This is the only one of our cases with antecedent acute appendicitis. We have also seen 1 or 2 cases which strongly suggested a congenital origin and verified a suspicion of the correctness of Keiller's, also Cotte's, omental idea. Also a few cases with alternating constipation and diarrhea have led us to suspect a coincident colitis, as believed by A. G. Gerster. In quite a larger percentage of cases,

<sup>1</sup> See articles on Fetal Peritoneal Folds by J. R. Eastman, *Journal of the American Medical Association*, August 30, 1913, p. 635.

<sup>2</sup> Cited by Eastman and Cole, *Annals of Surgery*, January, 1914, p. 45.

<sup>3</sup> *Annals of Surgery*, March, 1913, p. 374.

however, we are of the opinion that the view suggested by Dr. Hall is correct." (The specimen examined by Hall was obtained from a patient with pericolitis, dying from other causes. Microscopic section of the entire thickness of the wall of the colon showed a very loose external covering, a normal musculature, a broad submucosa, and a normal glandular coat. The serous coat seemed to have had its fibers split asunder, as if by a serous infiltrate, thus lifting the endothelial layer of the membrane. The bloodvessels were unusually large and thin-walled. Whenever a bloodvessel crossed, there was a condensation of the white fibers into bands parallel to it. In other words, there was a mass of more or less isolated fascicles of white fibrous tissue, with here and there a bloodvessel, with broad clefts lined with endothelium between. There were no evidences of recent acute inflammation. However, it was noted that the connective tissue next to the layer of the longitudinal muscular coat was condensed and seemed to penetrate in increased amount between the muscular bundles.)

Jackson goes on to say, "When we reflect that the area of gut most affected is that from which most of the physiologic absorption takes place in the normal tube, it is not difficult to assume that through this segment, mild infection and toxins may likewise pass from the peritoneum with necessarily concomitant inflammation of the mucous lining, though the latter may and doubtless often does, coexist." Jackson quotes the opinion of Harris, who is an advocate of the inflammatory theory, and who utilizes the work of Runeberg and Heyde upon anærobic bacteria as the basis for his belief.

This is supported by J. R. Eastman,<sup>1</sup> who *experimentally produced pericolic membranes* in rabbits by inducing a low-grade plastic peritonitis. A mild and easy peritonitis occurred as a result of plugging the large intestine with its own contents. Extreme coprostasis was induced by intermittent ligation of the anus and administration of morphine over a period varying from two weeks to three months. Like Jackson, Eastman also believes that several factors entered into the causation of pericolic membrane; in short, that there are both congenital and inflammatory origins for the structure, each of which may operate singly, or in combination with the other.

Referring to those of inflammatory origin, Eastman says,<sup>2</sup> "From my observation it appears that extensive membraniform adhesions may result from extreme coprostasis, and this is exactly as we should expect, for we know that incarceration of hernia and other forms of obstruction of the intestinal lumen, without visible lesion of the intestinal wall and without strangulation, lead to mild peritonitis, fusion and membraniform adhesions. Such pericolic membranes are not different in histology and origin from similar membranes around the

<sup>1</sup> Surgery, Gynecology, and Obstetrics, February, 1914, p. 228.

<sup>2</sup> Journal of the American Medical Association, January 24, 1914, p. 324.

uterus and uterine adnexa, all representing reaction of the peritoneum to irritation."

**TREATMENT.** According to Jackson, "The primary effort should be to relieve constriction, and the extent of dissection of the membrane should be governed by this necessity alone." He cites 2 cases, reoperated at the end of six months and one year, respectively, in which, at the primary operation, the colon was stripped of its pericolic membrane; at the second operation, no adhesions whatever were found. Among other procedures, Jackson suggests (1) reefing (plication) for a greatly dilated cecum, (2) an operation similar to that of Finney's pyloroplasty, for angulation at the hepatic flexure, and (3) a side-to-side cecosigmoidostomy as advocated by Yeomans in the *American Journal of Surgery*, January, 1913.

**The Late Results of Ileosigmoidostomy** are not uniformly successful, a fact to which I have called attention in previous years. The articles by Delbet,<sup>1</sup> Beck,<sup>2</sup> Pauchet,<sup>3</sup> Wilms,<sup>4</sup> Werelius,<sup>5</sup> and others,<sup>6</sup> all show that ileosigmoidostomy *per se* is not an entirely satisfactory operation. The surgeons of greater experience remove the blind colon proximal to the point of implantation of the small intestine, while some of lesser caliber hold to the fallacious idea that, if the small intestine is only implanted low enough down in the rectum, the normal antiperistalsis will not carry fecal material back to the partially excluded portion.

Kellogg<sup>7</sup> cites a case in which ileosigmoidostomy failed to relieve the patient's symptoms. At the second laparotomy many adhesions were found around the lower small intestine, which was so greatly distended that for some distance up from its junction with the colon, it was fully as large as a normal colon.

**Artificial Ileocolic Valve.** To prevent this regurgitation into the ileum, Kellogg devised an end-to-side anastomosis of the small intestines with the colon, in which the tube of small intestine projects into the lumen of the colon a distance of 2 to 3 cm., forming a valve. In a patient who died of an acute pneumonia several weeks after this operation, the valve was found to be perfectly competent. The accompanying figures explain the different steps of the operation (Figs. 69, 70, 71, and 72).

Drummond<sup>8</sup> studied the RELATION BETWEEN THE SMALL BOWEL AND THE COLON in some 5 or 6 cases of ileocolostomy. He used barium sulphate enemas. (The operation consisted in dividing the lower

<sup>1</sup> Bull. et mém. de la soc. de Chirurg. de Paris, 1913, No. 22, p. 911.

<sup>2</sup> Bruns, Beitr. z. klin. Chir., 1913, Band 84, p. 339.

<sup>3</sup> Bull. et mém. de la soc. de Chir. de Paris, 1914, vol. xxxix, No. 27, p. 1144.

<sup>4</sup> Zent. f. Chir., No. 16, 1913, p. 603.

<sup>5</sup> Surgery, Gynecology, and Obstetrics, 1913, vol. xvii, p. 510.

<sup>6</sup> See also Lyon Méd., 1913, vol. exxi, No. 44, p. 725.

<sup>7</sup> Surgery, Gynecology, and Obstetrics, November, 1913, p. 564.

<sup>8</sup> British Medical Journal, January 31, 1914, p. 240.

end of the ileum and implanting its proximal end into the pelvic colon lower down.) Where the operation had been done within a

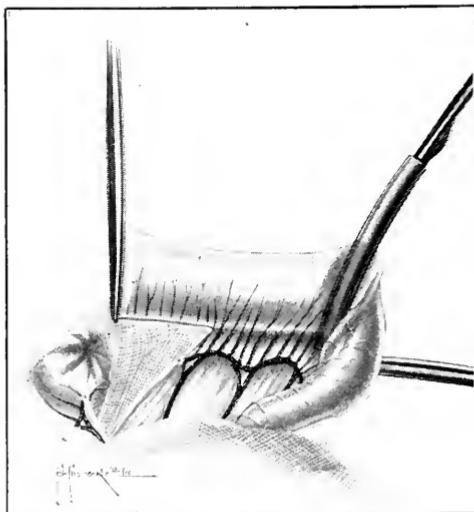


FIG. 69.—Kellogg's artificial ileocecal valve. Mesentery separated from end of ileum.

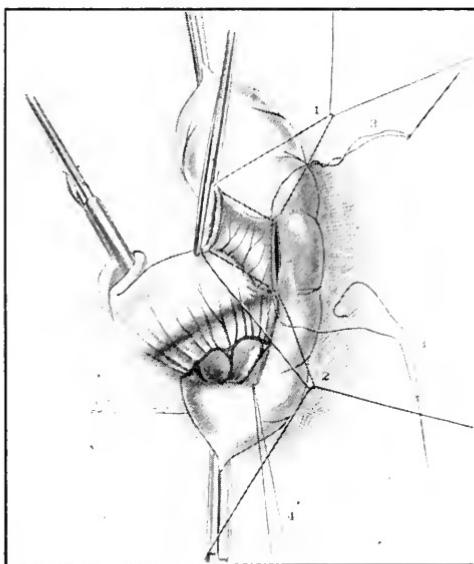


FIG. 70.—Kellogg's artificial ileocecal valve. Incision of colon preparatory to application of inner suture line.

month, the enema was seen to travel up the large intestine, and once as far as the cecum, but there was no indication that it entered

the small bowel. On the other hand, where the operation had been performed one or two years previously, the solution ran up into

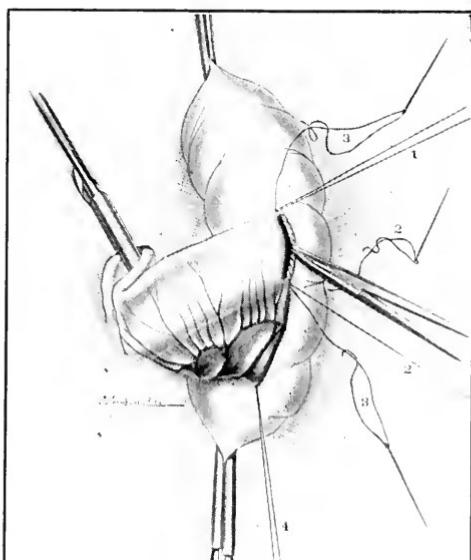


FIG. 71.—Kellogg's artificial ileocecal valve. End of ileum invaginated into the colon.

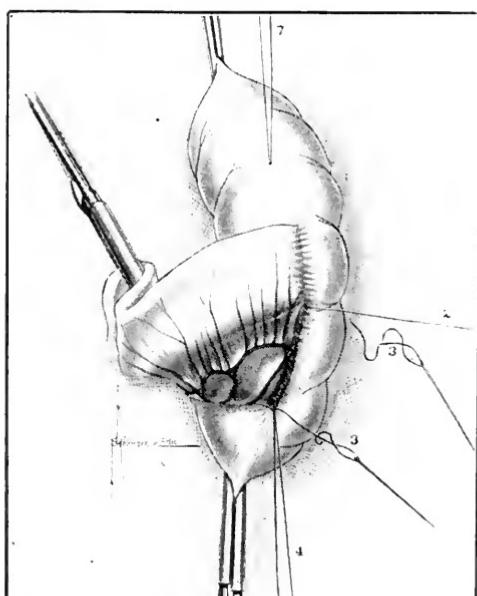


FIG. 72.—Kellogg's artificial ileocecal valve. Operation completed by attaching a portion of the mesentery to colon to prevent contraction at the point of anastomosis.

the small bowel, and was seen in distended loops of small intestine lying upon the right side of the abdomen; not until a considerable amount of the fluid was so disposed, did the large intestine proximal to the anastomosis begin to show a shadow. Drummond believes that, as time goes on, the dilated coils of small intestine adjacent to the colon assume somewhat the functions of the large gut. Be that as it may, it seems though ileosigmoidostomy, instead of relieving stasis in the lower end of the small intestine as well as in the large bowel, insures and exaggerates it.

**Incompetency of the Ileocecal Valve.** It is best to be guided by Carman's statement<sup>1</sup> that "in a fair proportion of cases, the opaque enema will go beyond the ileocecal valve into the ileum. Whether this incompetence has any pathologic significance is yet to be decided."

Kienböck<sup>2</sup> has found insufficiency of the ileocecal valve caused by ulceration, cicatricial deposit, etc.

Groedel<sup>3</sup> reports 22 cases of insufficiency of the ileocecal valve, 16 of which showed the clinical picture of chronic perityphlitis as just stated; the insufficiency can also be caused by ulcers, primary tumors, or metastases in this region.

Kellogg reports 30 cases of repair of an incompetent ileocecal valve, in every one of which subsequent *x-ray* examination showed the repaired valve to be absolutely competent. The accompanying figures illustrate the different steps of the operation (Figs. 73, 74, 75, 76, and 77). Kellogg emphasizes that care must be taken to avoid narrowing the opening too greatly. Time alone will tell whether either of Kellogg's plastics deserve a permanent place in intestinal surgery.

**The Roentgen Diagnosis of Ulcerative Colitis.** According to Stierlin, the affected portions of the intestine are free from large masses of bismuth and show only a few, long-drawn-out, streaked shadows of bismuth. The walls of the intestine run parallel to one another and show no haustral irregularity. They form the boundary of a particularly bright zone representing a collection of gas. This picture remains constant. Stierlin accounts for these findings by the oversensitive condition of the intestinal wall, which empties itself without delay, the bismuth remaining only in ulcers, diverticula, or longitudinal folds. The infiltrated wall has no haustral depressions. The findings of Schwartz and Novaceinsky agree with those of Stierlin.

Kienböck<sup>4</sup> examined 2 cases of tuberculous colitis and one of dysentery. He grouped the pictures obtained into two classes, one, in which the intestinal wall was still capable of movement. Here stretches of spastically contracted intestine often alternated with distended portions. The second type represented forms with rigid,

<sup>1</sup> Journal of the American Medical Association, August 2, 1913, p. 321.

<sup>2</sup> Fortsch. a. d. gebeit. d. Röntgenstrahlen, 1913, p. 231.

<sup>3</sup> Ibid., Band xx, Heft 2.

<sup>4</sup> Ibid., 1913, Band xx, Heft 3, p. 231.

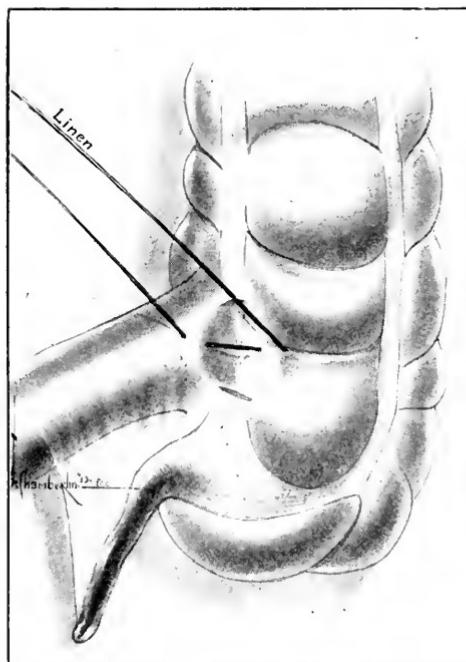


FIG. 73.—First step in repair of incompetent ileocecal valve. Suture placed to restore posterior lip. (Kellogg.)

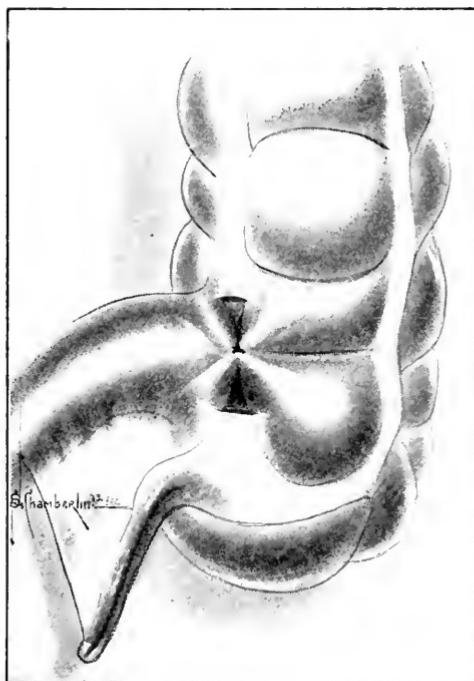


FIG. 74.—Suture tied. (Kellogg.)

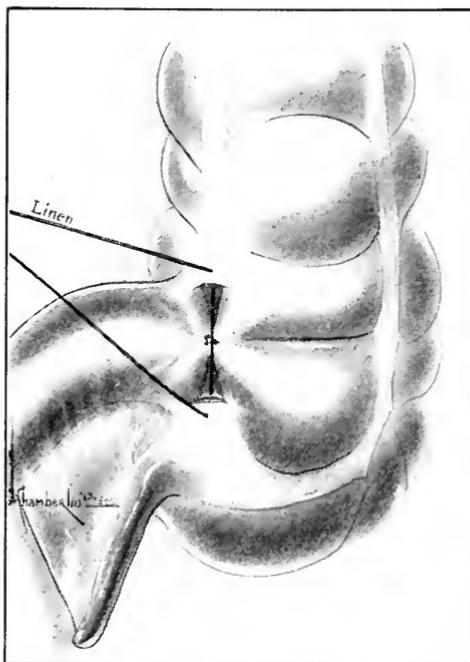


FIG. 75.—Second suture placed to approximate ends of the torn habenula.  
(Kellogg.)

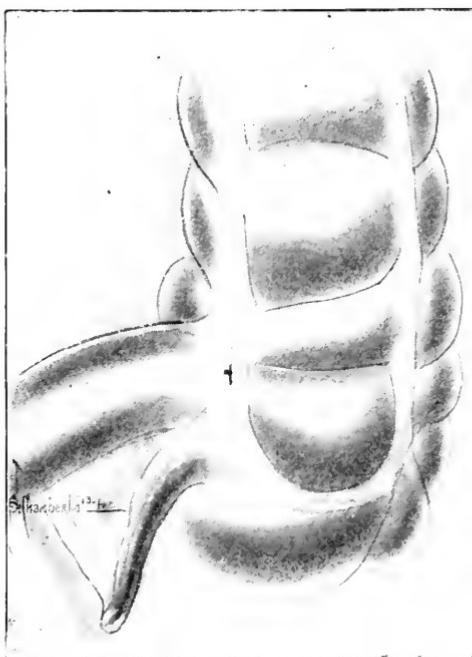


FIG. 76.—Suture tied. Repair of valve completed. (Kellogg.)

infiltrated walls, and ulcer formation. Here the gut constituted a cylinder filled with air, its margins showed slight angular irregularities. Upon administration of a bismuth enema, the first form showed a small narrowed tube, the second a wide cylinder with ulcerated excavations at its margin. The inflammatory changes around the ileocecal valve often rendered it incompetent.

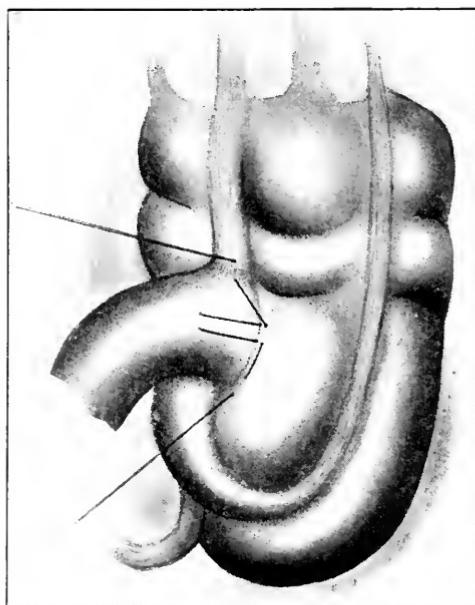


FIG. 77.—Method of repairing valve by means of a single suture. (Kellogg.)

**The X-ray Demonstration of Hirschsprung's Disease by Air Inflation.** Frank's<sup>1</sup> patient was a boy, aged fourteen years, who showed symptoms of Hirschsprung's disease. After a bismuth meal, while the *x*-ray picture showed widening of the large intestine, it was not possible to determine the exact size or location of its different parts. However, when the large intestine had been completely emptied by enemas and irrigations, and was then distended with air by means of a rectal tube, *x*-ray plates clearly demonstrated both limbs of the enormously distended sigmoid, the kink where it joined the rectum, and distention of the ascending colon.

**Volvulus of the Entire Small Intestine, Cecum, and Ascending Colon.** This rather rare condition was reported by Zahn,<sup>2</sup> at autopsy upon a child of six years dying with symptoms of intestinal obstruction, it

<sup>1</sup> Mitt. a. d. Grenzgeb. d. Med. u. Chir., Band xxvi, Heft 1.

<sup>2</sup> Diss. Erlangen, 1913; Zent. für die gesamte Chir. u. i. Grenzgeb., 1913, Band i, No. 12, p. 596.

was found that lack of fixation of the ascending colon and cecum (which had a common ileocecal mesentery) had made the occurrence of such a volvulus possible. To this are added 15 other cases from the literature.

**Multiple Acute Perforation of the Small and Large Intestines** is an unusual condition the etiology of which is very little known. The patient of DeRouville and Roger<sup>1</sup> was a woman, aged forty-five years, upon whom a hysterectomy had been done for sclerosing metritis. All went well until the eighteenth day after operation when there was a sudden attack of abdominal pain and profuse diarrhea without blood. During the following days there was nausea but no vomiting, a soft abdomen, rapid pulse, very slight fever, and constant diarrhea which could not be controlled by therapeutic measures. Typhoid fever was suspected. The tongue was dry, the abdomen distended but soft, there was tenderness in the right lower quadrant, no icterus. A steadily downward course ended in death upon the fourth day. At autopsy, darkly stained omentum was found adherent to a mass of distended loops of small intestine. In these and in the cecum were about fifty perforations varying in size from a pinpoint to that of a ten-cent piece. Both within the intestines and without, was foul, yellow fluid containing bubbles of gas. The perforations and adjacent ulcerations lay with their long axes circular to the lumen of the intestine. Their location did not correspond to that of the Peyers patches. Both macro- and microscopic examination seemed to indicate that the destruction began in the mucosa. There were no emboli of the large arteries. Immediately adjacent to the ulcers, the lumina of the vessels were found crowded with small bacilli. Findings in the other organs were of no significance.

This case probably belongs in the same general category as acute perforations of the cecum and ascending colon diagnosed as acute appendicitis previous to operation.

**Carcinoma of the Colon.** The Cavendish Lecture of Moynihan,<sup>2</sup> and the reports of Bastianelli<sup>3</sup> and Körte,<sup>4</sup> at the International Congress in London last summer, are the most important communications on this subject appearing during the past year.

They go into the subject in such detail and with so many statistics that their articles do not readily lend themselves to a short review. However, one or two of Moynihan's technical observations are not out of place here. He states that marginal necrosis because of insufficient blood supply is a myth (apparently inferring thereby that if it does occur, it is due to pulling of the stitches too tightly). He makes an

<sup>1</sup> Rev. Prat. d'obstetr. et de gynecol., 1913, p. 102.

<sup>2</sup> Lancet, 1913, vol. clxxxv, p. 1. West London Medical Journal, 1913, vol. xviii, No. 3, p. 165.

<sup>3</sup> Rivista Osp., October 31, 1913, p. 77.

<sup>4</sup> Zent. f. d. gesamte chir. u. i. Grenzgeb., vol. iii, p. 188.

end-to-end anastomosis after resection, provided the intestine is entirely surrounded by serosa. Otherwise, he performs a side-to-side anastomosis.

THE SITE OF ELECTION FOR COLOSTOMY will always remain a matter for discussion. Two authors differ from the commonly accepted view that a left iliac colostomy is the most suitable.

McGavin<sup>1</sup> reports 26 cases of transverse colostomy since 1906. As advantages of this method, McGavin cites absence of involuntary escape of feces, or of prolapse of intestinal mucosa, because there is no column of fecal material situated higher than the opening, as in an iliac colostomy. Furthermore, in fat people, the transverse colon is more accessible than the sigmoid. McGavin denies that his method has any disadvantages, such as the escape of stool from a part of the intestine where it is still fluid, insisting that ignorance of the advantages of his method and the inherent conservatism of operators, have prevented its widespread adoption.

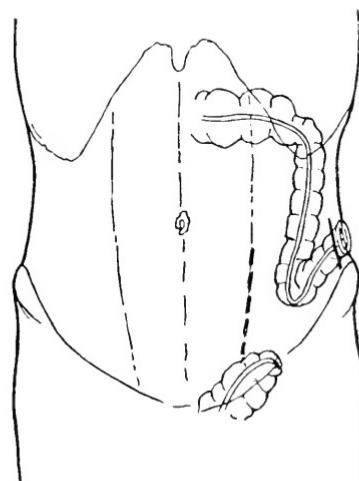


FIG. 78

Brenner<sup>2</sup> recommends the establishment of a permanent colostomy well over in the flank, just above the iliac crest (Fig. 78), bringing down the intestine through a gridiron incision, thus permitting two layers of muscle to act as sphincters. Brenner's case dates back seventeen years (1896) and have given complete satisfaction.

Among other advantages, he claims that fixation of the colostomy to the flare of the ileum makes it easier to keep the occluding pad from slipping—than in the case of the usual iliac colostomy. Brenner

<sup>1</sup> British Medical Journal, May 10, 1913.

<sup>2</sup> Zent. f. Chir., 1913, p. 1950.

expressly disclaims any statement that this method is new. Indeed, he gives a very complete list of references of those who first conceived the idea of establishing a colostomy in this region, of employing the muscular abdominal wall as a sphincter, and so on. He believes this method is indicated after total extirpation of the rectum and sigmoid where there is not enough colon left to bring it down to the anal region, as well as for cases of inoperable carcinoma of the rectum. The well-known principle of establishing a U-shaped loop to act as a sort of ampulla is also made use of by him.

POINTS IN THE SURGICAL ANATOMY OF THE RECTUM which are of distinct practical value in carrying out its extirpation, are dwelt upon by J. W. Smith.<sup>1</sup>

The chief factor in preventing mobilization of the rectum are its lateral supports, and Smith points out that one may divide the tissues in the median line from the perineum to the peritoneum and yet not be able to move the rectum more than an inch or two from its original position. This is prevented by laterally placed attachments of the rectum to the sacrum (its third and fourth segments) by the transversely running rectal fascia, by the connective-tissue strands encircling the rectal branches of the second, third, and fourth spinal nerves, and by branches of the superior hemorrhoidal arteries. After division of the lateral attachments, as much as eighteen inches of the rectum can be pulled down.

CARCINOMA OF THE RECTUM. Certain interesting findings which in part support the contentions of Handley regarding carcinomatous spread, are reported by Cole<sup>2</sup> in his series of 20 cases of adenocarcinoma (18 were specimens obtained by operation, 2 by autopsy). It was found that the tumors usually take their origin from the anterior or lateral wall. There seems to be a tendency to circular rather than to longitudinal spread, for, even in those cases where apparently a complete circular involvement of the gut had occurred, microscopic examination showed that the median part of the posterior wall was not involved. After discussing other pathologic details of carcinomatous spread, Cole cites an example showing how impossible it is to tell the extent of distal involvement from the local findings. Fourteen inches above the primary tumor, the intestinal mucosa was seen to be atrophic. Microscopic examination showed the lymphatics beneath the submucosa, and between it and the circular and longitudinal muscular layers, crowded with carcinoma cells.

**The Whitehead Operation for Hemorrhoids.** Reports on the late results of this operation by Stone<sup>3</sup> (470 cases); Nolan Lloyd<sup>4</sup> (200 cases);

<sup>1</sup> Journal of Anatomy and Physiology, 1913, p. 350.

<sup>2</sup> British Medical Journal, 1913, p. 431.

<sup>3</sup> Annals of Surgery, November, 1913, p. 647.

<sup>4</sup> Surgery, Gynecology, and Obstetrics, vol. xvi, p. 213.

and Hadda<sup>1</sup> (223 cases), would seem to show that this method gives excellent results if properly performed, and that the wide disrepute into which it has fallen because of the likelihood of incontinence and stricture formation, which were quoted as frequent sequelæ, was due to the lack of proper technique, rather than to any inherent defect in the operation itself.

### THE LIVER.

**The Functional Importance of the Gall-bladder.** Rost<sup>2</sup> found that the bile, which escapes into the duodenum during digestion, is derived from the supply stored up in the gall-bladder bile and passages, and is not the result of reflexly increased activity of the liver. In dogs during the first weeks after cholecystectomy, bile and pancreatic secretion continuously escaped into the intestine. It naturally followed that, during digestion, the dog without the gall-bladder secreted only one-third as much bile and pancreatic juice as the normal animal. There was no change in the nitrogen or fat metabolism of the operated animal. Anatomical investigation, both in man and animals, showed that the presence of a long sphincteric muscle at the papilla of Vater gave rise to dilatation of the bile passages within a few weeks after operation. Under such circumstances, if part of the cystic duct was left behind, it developed into a new gall-bladder. Rost demonstrated such a gall-bladder eighteen months after cholecystectomy. On the other hand, a short sphincter was associated with no dilatation of the bile passages, but frequently there was inflammation of the bile passages.

**Anomalies of the Gall-bladder and Hepatic Artery** having surgical importance are cited by Kehr.<sup>3</sup> Among these are absence of the gall-bladder, its intrahepatic position, its displacement to the left, a doubling of the hepatic duct, in which case one of the two ducts may open directly into the gall-bladder or into the cystic duct. The right branch of the hepatic artery may originate from the superior mesenteric artery, in which case a hemorrhage from it would not be stopped by a ligation of the hepatic artery. The cystic artery may originate from the gastroduodenal. There may be two cystic arteries, one of which (on the right) arises from the hepatic artery, the other from the gastroduodenal.

**Bradycardia as a Sign of Injury of the Liver,** was brought forward some time ago by Finsterer. Rubaschow<sup>4</sup> denies the special significance of this symptom and cites 35 clinical cases of bradycardia following almost all types of abdominal injury. Finsterer<sup>5</sup> replies in a rather rambling fashion, and ends with the statement that a full, slow pulse

<sup>1</sup> Langenbeck's Archiv., vol. c, Heft 4.

<sup>2</sup> Mitt. a. d. Med. u. Chir., Band xxvi, Heft 5.

<sup>3</sup> Zent. f. Chir., 1913, p. 690.

<sup>4</sup> Deutsch. Zeitsch. f. Chir., Band exxi, p. 515.

<sup>5</sup> Loc. cit., p. 520.

does not exclude the diagnosis of internal hemorrhage from rupture or injury of the liver.

**Methods of Obtaining Hemostasis** at operation for injury of the liver or while performing a resection, has been mentioned in my previous articles. Of these, the best is compression of the hepatic artery and portal vein in the free edge of the lesser omentum; it, however, has the disadvantage that it leads to great lowering of the general blood-pressure and to hemorrhagic infarction of the intestine as a result of the portal stasis. To prevent this, Oppel<sup>1</sup> suggests simultaneous compression of the abdominal aorta and the portal vein, as a means for preventing overdistention of the portal system with venous blood.

The various means for controlling oozing from the liver have been referred to at the beginning of this article (see p. 74).

**CHOLEMIC HEMORRHAGES.** In the present state of our knowledge, when hemophilic conditions are proving readily amenable to either subcutaneous or intravenous administration of normal blood or normal serum, it is surprising to read the out-of-date remarks of Kehr,<sup>2</sup> who states that "neither calcium chloride nor horse serum, neither gelatin nor sugar solution, are of any value in this condition." While no one doubts that prevention in the shape of timely operation, as stated by Kehr, is the best means of combating the condition, deeply jaundiced cases will always come to the surgeon long after operation should have been done, some of these will bleed, and this bleeding can be stopped either by the administration of horse serum, or, better, defibrinated blood subcutaneously or, best of all, by transfusion.

**Implantation of the Superior Mesenteric Vein into the Vena Cava for the Relief of Portal Obstruction** in cirrhosis of the liver was performed by Bogoras.<sup>3</sup> Close to the duodenojejunal junction, the superior mesenteric vein was isolated, its lower part was freed and the central end was ligated. Beyond the point of ligation, a number of large branches joined the remainder of the vein to form the portal trunk so that some of the blood still went to the liver. The vena cava was now exposed, a curved clamp was applied to its lateral walls, and the peripheral end of the mesenteric vein was implanted into a transverse opening in the cava. Convalescence was uneventful except for a transient oliguria. The patient remained under observation for one month after operation, the spleen became smaller and the amount of fluid in the abdomen did not increase.

**The Confusion of Acute Congestion of the Liver with Gall-stone Colic.** Ortner<sup>4</sup> says that the severe pain accompanying acute congestion of

<sup>1</sup> Zent. f. Chir., 1913, p. 218.

<sup>2</sup> Verhandl. d. Deut. Gesellsch. f. Chir., 1913; see also Zent. f. Chir., 1913, p. 76, No. 28.

<sup>3</sup> Russki Wratsk, 1913, No. 2.

<sup>4</sup> Medizinische Klinik, September 21, 1913.

the liver from insufficiency of the right heart may be mistaken for gall-stone colic. He tells of a man, aged fifty-two years, whose recurring attacks of severe pain back of the sternum and in the upper abdomen found no ready explanation. There was moderate dilatation of the heart with signs of chronic, mild myocarditis and some arteriosclerosis. While puzzling over this case, another patient presented himself with the same clinical picture. He, however, stated that his pain came on after climbing a hill. Ortner then had the first patient climb a hill, and this promptly brought on an attack. During the attack of pain the liver was found enlarged to the umbilicus. Rest in bed for a few days afforded complete subjective recovery to both patients. A third patient also exhibited the same symptoms.

A similar case seen by von Brunn,<sup>1</sup> previous to the appearance of Ortner's publication, led to the performance of an exploratory laparotomy. A sixteen-year-old miner had an attack of abdominal pain, which, however, did not prevent his keeping on at work all that day and the one following. The third day, as he was going to work, his abdominal pain increased to such an extent that he returned home. There was vomiting and sweating. His condition became so alarming that the local doctor referred him immediately to the hospital, to the medical side of which he was admitted. He was then promptly transferred to the surgical side. Examination showed a well-developed boy, groaning with pain, with pale face, and livid lips. In short, there were all the physical signs of an intense collapse. The heart was not enlarged, the sounds faint but clear, at the wrist the pulse was twenty-two, of poor quality, and irregular rate. Upon auscultation, between the strong beats were heard weak contractions, which failed to give any pulse at the wrist. The lungs showed nothing abnormal. The abdomen was retracted, its upper half was abnormally sensitive and rigid; the lower abdomen was not sensitive. There was dulness in the right upper abdomen, reaching to the navel. The diagnosis was not clear. Inasmuch as perforation of the stomach, with a circumscribed exudate could not be excluded, it was deemed wise to perform an exploratory laparotomy under ether. Upon opening the abdomen, an enormously enlarged liver was found corresponding to the region of dulness and tenderness. The spleen was enlarged and hard. There were no signs of inflammation. Following operation, the pulse improved, the pain subsided, and the liver dulness diminished to within its normal limits. However, on the eleventh day after operation, an increase in cardiac dulness was found to reach a finger's breadth beyond the left nipple. There was a systolic murmur audible over the entire heart which varied in intensity. Nine days later it was barely audible.

<sup>1</sup> Zent. f. Chir., 1913, p. 1661.

**Other Conditions Mistaken for Gall-stones** are reported in Lejar's<sup>1</sup> instructive paper. Thus, perigastritis in the neighborhood of the pylorus with its adhesions have been known to cause symptoms typical of gall-stone disease. Cirrhosis of the liver may develop with colicky pains, jaundice, and tenderness in the gall-bladder region, as was shown in a woman, aged thirty-nine years, in whom operation revealed a normal gall-bladder with an irregular, soft, yellowish liver. A similar case recently occurred in the service of A. G. Gerster at Mount Sinai Hospital. A man of middle age was admitted to the surgical ward with a diagnosis of cholecystitis. After several days' observation, he was transferred to the medical ward with the diagnosis of cirrhosis. After several weeks' sojourn there, he was again returned to the surgical ward with the diagnosis of [REDACTED]. Laparotomy revealed a normal gall-bladder and bile passages, and a typical (hob-nail appearance) cirrhosis of the liver.

Among other cases of Lejar's were two of echinococcus cyst simulating gall-stone trouble. A large gumma of the liver was perplexing at first because the Wassermann reaction was negative; later, the Wassermann turned positive.

**Emetine in Amebic Diseases of the Liver.** During the past year, all the statements made by Rogers regarding the treatment of amebic liver abscess have received ample confirmation. In Vedder's excellent review of the entire subject, it is pointed out that while the cases are invariably cured of their symptoms, many individuals continue to have amebae in their stools. This fact, however, is of greater medical than surgical interest.

**The Treatment of Typhoid Carriers by Cholecystectomy** does not invariably cure this condition. Unfortunately, cholecystectomy is not always followed by disappearance of the bacilli as reported in the 2 cases of Leary.<sup>2</sup>

**Does a Biliary Peritonitis Exist Without Perforation of the Bile Passage?** The affirmative position taken by Clairmont and von Haberer has been questioned by Nauwerck and Lubke<sup>3</sup> because of the findings in a case of theirs. At laparotomy upon a man, fifty-six years of age, large amounts of bile were found in the abdominal cavity. The gall-bladder was distended. No perforation of the bile passages was demonstrable either at that time or at the autopsy later on. There were, however, erosions of the mucous membrane of the gall-bladder. Only by microscopic examination of these erosions was it shown that tiny perforations existed. In another case of bile in the abdominal cavity, a pinpoint perforation covered with fibrin was found on the surface

<sup>1</sup> Semaine Médicale, November 26, 1913.

<sup>2</sup> Journal of the American Medical Association, vol. ix, No. 17.

<sup>3</sup> Berliner klin. Woch., 1913, No. 14.

of the right lobe of the liver; it communicated with a distended sub-serous bile capillary.

In their answer, Clairmont and von Haberer<sup>1</sup> concede that the bile may leak through such microscopic openings and escape observation even at autopsy, but maintain that the clinical problem remains the same, namely, that it is impossible for the surgeon to locate the place where the bile is making its escape.

Sven Johansson<sup>2</sup> reports such a case in a woman, aged seventy-six years. Even at autopsy, it was not possible to find either a perforation or ulceration of the biliary system. Johansson reports four other cases of biliary peritonitis without perforation of the bile passages. In two of these there was choledolithiasis; one followed trauma without visible perforation. (There was no air<sup>3</sup> in the duodenum or small intestine); one occurred in a typhoid. In discussing the etiological possibilities of this phenomenon, Johansson mentions that the canals of Luschka might play a certain role, although up to the present time microscopic evidence is lacking. Such a rupture has actually been demonstrated by Sick and Fraenkel.<sup>4</sup> A pinpoint perforation of the gall-bladder was recognized at operation. Instead of closing this by suture, the gall-bladder was extirpated because it was feared that even if this were done other perforations might occur.

Similar cases of biliary peritonitis without demonstrable perforation of the bile passages are reported by Soelling,<sup>5</sup> Askanazy,<sup>6</sup> and Favreul.<sup>6</sup>

Vogel<sup>7</sup> tells of 2 cases. One recovered; the other died. At autopsy on the latter, the rupture of a superficially located distended bile capillary was found.

In repeating the animal experiments of Clairmont and von Haberer (ligation of the common bile duct), Vogel noted that bile was found in the peritoneal cavity only in those cases where the ligature had cut through.

**Aschoff's Theory of the Formation of Gall-stones** was brought out some time ago. It has gained wide acceptance. A recent review of this theory with additional proofs has been published by Baemeister,<sup>8</sup> the assistant of Aschoff's who aided his chief in the original investigation and whose name also appears as co-author. According to this theory, the formation of stone results, (1) from stasis in the bile passages and consequent disintegration of the bile; and (2) from increase in the cholesterolin content of the bile as shown by recent investigations. This condition is present in diabetes, adiposity, atherosclerosis, chronic nephritis,

<sup>1</sup> Wiener klin. Woch., 1913, p. 891.

<sup>2</sup> Reone de Chir., XXII annee, No. 12, and Hygila, vol. lxxv, Heft 4, p. 392.

<sup>3</sup> Bruns, Beitr. z. klin. Chir., Band elxxxv, Heft 3, p. 687; Zent. f. Chir., 1914, p. 17.

<sup>4</sup> Hospital stidendeude, 1913, No. 4.   <sup>5</sup> Berliner klin. Woch., 1913, No. 36.

<sup>6</sup> Rev. fran. Med. et de Chirurg., 1914, p. 217.

<sup>7</sup> Berliner klin. Woch., 1913, p. 1156.

<sup>8</sup> Ergeb. d. inn. Med. u. Kinderheilk., 1913, Band xi, p. 1.

pregnancy, the puerperium, lactation, typhoid fever, etc. Aschoff and Baemeister distinguish between an inflammatory and non-inflammatory stone formation. The non-inflammatory formation of stone comes to pass as a result of stasis of the bile and increase in its concentration.

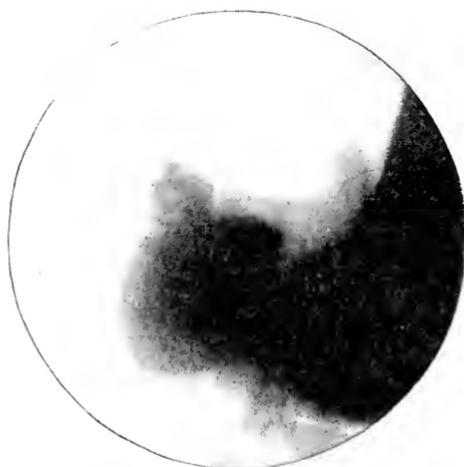


FIG. 79.—Contraction of cap and pars pylorica by adhesions from cholecystitis with calculi invisible Röntgenographically. Proved by surgery. (Cole.)

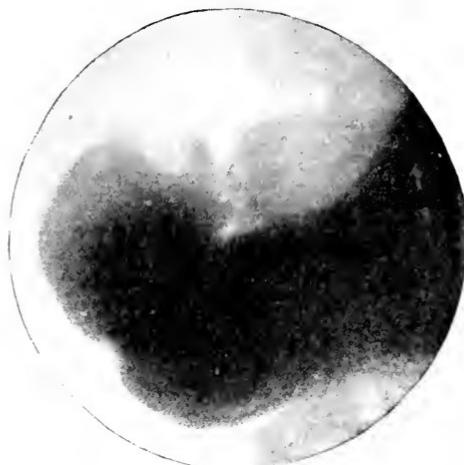


FIG. 80.—Absence of cap. Sphincter widened on lesser curvature. Cholecystitis with calculi invisible Röntgenographically. Proved by surgery. (Cole.)

The pure cholesterol stones blocking the neck of the gall-bladder are formed in this way. They are not the result of inflammation. They, however, give rise to stasis and this predisposes to infection of the bile passages. If this occurs, a chronic recurring cholecystitis may develop. Stone formation, therefore, is never a primary disease; it is always

secondary. Therapy must include not only removal of the stones, but must also provide for a good biliary drainage, diminution of cholesterin formation and healing of the existing inflammation of the biliary system. A typical example of the two types of stone is shown in a gall-bladder



FIG. 81.—Indentation in greater curvature, in which lay small, atrophic gall-bladder, containing calculus invisible Röntgenographically. Proved by surgery.

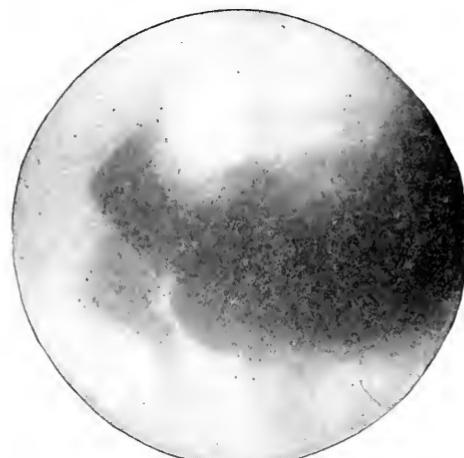


FIG. 82.—Adhesions of cap and pars pylorica from cholecystitis. No calculus visible Röntgenographically. Surgery imminent.

whose neck is blocked by a pure cholesterin stone, while the rest of the gall-bladder is filled with innumerable, dark brown, faceted stones containing bile pigment as well as cholesterin. This former is the result of overconcentration of the bile, the latter, of inflammation. The so-called combination stones have a pure cholesterin nucleus around which

is a deposit of bile pigment in combination with salts. In those cases where no cholesterol stones are found, it is reasonable to suppose that they have been passed out, leaving behind only the stones of inflammatory origin. For further details and support of this theory see the most recent communication of Aschoff.<sup>1</sup>

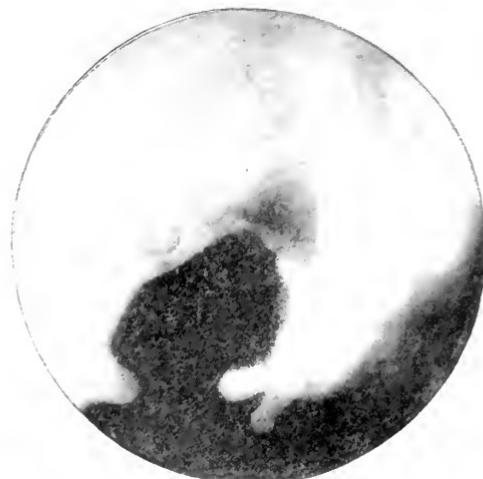


FIG. 83.—Pressure on terminal wave and cap by four gall-stones. Anterior view. Proved by surgery. (Cole.)



FIG. 84.—Adhesions of cap and pars pylorica from cholecystitis with five calculi. Anterior view. (Cole.)

The Röntgenographic Diagnosis of Gall-stones and Cholecystitis is outlined by Cole<sup>2</sup> in an extremely instructive paper. Cole divides the obtainable evidence into two classes—indirect and direct.

<sup>1</sup> Münch. med. Woch., 1913, No. 32, p. 1753.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, February, 1914, p. 218.

*Indirect Evidence* is afforded by the distortion of the adjacent hollow viscera by adhesions from cholecystitis (Figs. 79, 80, 81, and 82). Cole says, "I believe that the deformity of the cap and pars pylorica or the kinking and constriction of the hepatic flexure are stronger Röntgenologic indications for surgical procedure than the presence of a calculus in the gall-bladder, without evidence of adhesions involving the hollow viscera."

*Direct Evidence.* Gall-stones and cholecystitis were demonstrated Röntgenographically in 20 out of 500 cases examined for gastro-intestinal lesions (Figs. 83 and 84). An intensifying screen and soft tube were used with a very short exposure. Naturally, the detection by the x-ray depends upon the percentage of mineral salts in the stone.

The following differential points between biliary and renal calculi must be borne in mind.

1. Biliary calculi show more distinctly and appear smaller when the plate is placed on the abdomen than when it is placed on the back. The opposite is true of renal calculus. With calculi in the cystic duct, variation in size is not so great. Here comparison between a number of plates taken from different positions in front and behind must be made.

2. Renal calculi are seldom, if ever, met, the ring-like shadow of a biliary calculus having a calcareous coating outside of a cholesterol nucleus.

3. Biliary calculi are more likely to be faceted than are renal calculi. The latter are more frequently branched.

4. Moving the tube from side to side alters the relation of a biliary calculus to the kidney, but it does not alter the relation of a renal calculus to the kidney (Figs. 83 and 84).

**Gall-stones in Children.** Although Knautz<sup>1</sup> has been able to collect only 15 cases, it is very likely that the disease is not rare. At a recent meeting of the New York Surgical Society at least 6 cases were cited following the presentation of two patients previously operated upon for this condition.

The monographs of Thöle,<sup>2</sup> on **Injuries of the Liver and Bile Passages**, and **Surgery of Tumors of the Liver**, are the most important works of reference on these subjects at the present time. The *Billroth-Lencke Deutsche Chirurgie* and the recently started *Neue Deutsche Chirurgie*, together form the most valuable collection of surgical monographs in existence. At the time of publication each volume contains all the available knowledge of the particular subject, together with literary references of every important article published up to that date. It is a pity that we have nothing like it in the English language.

<sup>1</sup> Zent. f. d. Grenzgeb. d. Med. u. Chir., May 23, 1913.

<sup>2</sup> Chirurgie der Lebergeschwüste, Neue Deutsche Chirurgie, 1913, Band vii.

**Subserous Drainage of the Stump of the Cystic Duct after Simple Cholecystectomy.** Recognizing that both primary closure of the abdomen after simple cholecystectomy, and tamponade after this operation, have certain obvious disadvantages, Flörken<sup>1</sup> suggests subserous drainage of the stump of the cystic duct as a happy medium between the two aforementioned methods. After subserous removal of the gall-bladder and exploration of the bile passages, the cystic duct is simply ligated and this, together with a thin rubber drainage tube whose ends lies near it, are buried by uniting the peritoneum over them. The tube emerges from this subserous bed near where the fundus of the gall-bladder formerly lay. The abdominal wound is completely closed except where the tube comes through. The tube is removed on the fifth or sixth day.

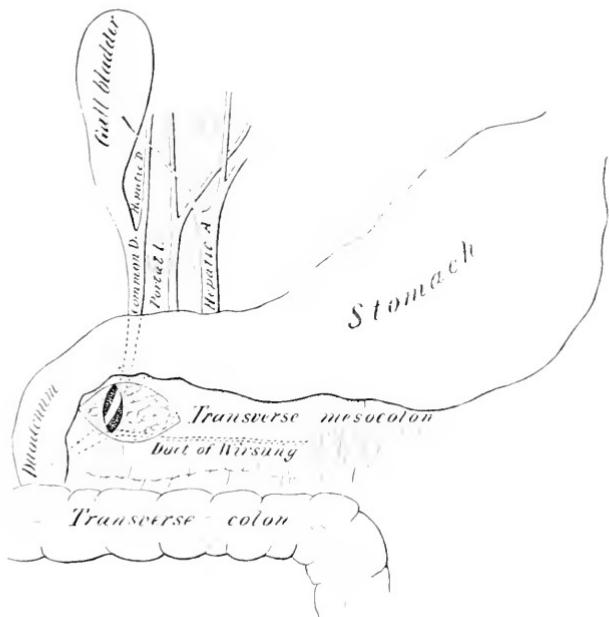


FIG. 85.—Transpancreatic choledochotomy. (Fink.)

**Transpancreatic Choledochotomy for Stone** is rarely attempted because the lower part of the common duct can usually be reached either by the transduodenal or the retroduodenal route. In the case of Fink<sup>2</sup> the impacted stone in the retroduodenal part of the common duct could be felt as a tumor which pushed forward the pancreas at the lower margin of the first portion of the duodenum. The accompanying illustration (Fig. 85) shows the transverse opening in the mesocolon, and the vertical incision of the pancreas, by which the impacted stone

<sup>1</sup> Zent. für Chir., 1913, p. 1516.

<sup>2</sup> Ibid., p. 1811.

was exposed. Tamponade of the pancreatic wound and drainage of the supraduodenal common duct. Up to the twelfth day after operation, all went well. Then a duodenal ulcer, 2.5 cm. from the pylorus, perforated and the patient died.

**The Late Results in the Various Plastic Methods Designed to Connect the Bile Passages with the Gut** are in the main, extremely unsatisfactory. Only too often does one read of a good postoperative result which is followed anywhere from three months to two or three years by recurrence of symptoms and the speedy death of the patient. Autopsy usually shows infection of the bile passages, with biliary abscesses throughout the liver.

When it was found that a drainage tube could safely be used to perform the functions of the common bile duct for many months, it was hoped that at last a method had been found in which physiological conditions were imitated closely enough to prevent an ascending infection. This has not proved to be the case, as illustrated by the report of Cahen.<sup>1</sup> A catheter leading from the hepatic duct was implanted into the stomach according to the method of Witzel. The patient died three months after this operation (the tube had been vomited up four weeks after operation). At autopsy, the liver was found studded with abscesses, the passage in the stomach wall had closed and there was an opening in the duodenum with which the hepatic duct communicated, Cahen believed this formed as a result of pressure necrosis from the catheter.

In Germany, the method of Völcker seems to have the preference at present.<sup>2</sup> In this the catheter, with its point in the cystic duct, is led into the duodenum or jejunum from which it emerges again through a Witzel fistula to reach the outside of the abdomen. A number of fenestra permit escape of bile into the intestine.

Kramarenko<sup>3</sup> suggests establishing a biliary fistula and a jejunostomy according to Witzel close to each other, and uniting their mouths by means of a drainage tube. For this method he claims the advantage that in case a cholangitis occurs, the connection between the intestine and the gall-bladder can immediately be discontinued.

The report of Propping<sup>4</sup> of a case where the defect of the common duct was bridged by means of a T-tube and in which he claims that the tube permitted regeneration of the duct's lumen, is not convincing. A stricture of the common duct recurred after the first employment of the T-tube, and at the date of publication not sufficient time had elapsed to indicate whether another stricture might not be forming.

<sup>1</sup> Deutsch. Zeitsch. für Chir., Band exxii, Heft 3, 4, p. 331.

<sup>2</sup> Anschütz, Zent. für Chir., 1914, p. 18; and Nordmann, Deutsch Gesellsch. für Chir., 1913.

<sup>3</sup> Zent. für Chir., 1913, p. 1263.

<sup>4</sup> Bruns, Beitr. z. klin. Chir., vol. lxxxiii, Heft. 2.

The employment of the gall-bladder as a means of bridging a defect in the common duct (Fig. 86), as suggested by Wolff,<sup>1</sup> has the advantage that the normal papilla affords a certain degree of protection against ascending infection.

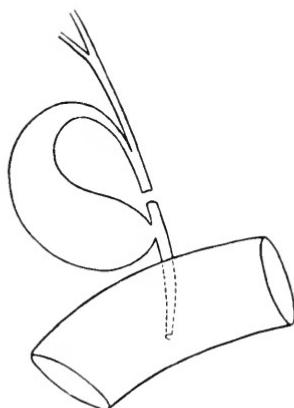


FIG. 86.—Employment of gall-bladder to bridge defect of common duct. (Wolff.)

A transplanted piece of vein has been suggested as a substitute for the common bile duct by Stropani and Giordano.<sup>2</sup> The attempts to use bloodvessels to bridge gaps in the ureter have invariably resulted in failure sooner or later. The transplanted vessel shrinks and becomes a mass of dense cicatricial tissue. I am sure the same result will be found in the case of the bile passages.

The newest and least practical suggestion of all, is that of Molineus,<sup>3</sup> who proposes to use the appendix as a substitute for the common bile duct. The fact that this transplantation takes one hour when performed upon the cadaver, is alone sufficient to condemn it.

#### THE PANCREAS.

**The Experimental and Clinical Relationship between Acute Necrosis of the Pancreas and Cholecystitis or Cholelithiasis.** At the 1913 meeting of the Deutsche Gesellschaft für Chirurgie, Nordmann, of Berlin, prefaced his remarks by referring to the well-known fact that in about 40 per cent. of the cases of acute hemorrhagic pancreatitis there is a coexistent cholecystitis or cholelithiasis. In many experiments dealing with the etiology on this condition, bile or infected bile, was injected into the pancreatic ducts. According to Nordmann, the acute necrosis of the pancreas, following this procedure, is brought about by rupture

<sup>1</sup> Zent. für Chir., 1914, p. 231.

<sup>2</sup> Ibid., p. 190.

<sup>3</sup> Deutsche Zeitsch. f. Chir., Band exxi, p. 427.

of the finest branches of the pancreatic ducts and a consequent forcing of pancreatic secretion into the tissues. Consequently this does not reproduce the probable processes in the human pathology.

In 30 dogs both papillæ of the pancreatic ducts were closed with sutures of silkworm gut, then a bacterial suspension was injected into the gall-bladder, the greatest care being taken to avoid any mechanical trauma to the pancreas. In 14 cases, a typical pancreas necrosis, with hemorrhages and extensive fat necrosis, was obtained, which, macroscopically and microscopically, corresponded to the condition found in man.

On the other hand, it was found that if the upper papilla was closed and the lower one left open, no infection of the pancreas ensued in spite of the inflammation present in the bile passages. Similar negative results were obtained when both papillæ were ligated, the lower one in such a manner that the common bile duct did not communicate with the pancreas. Nordmann considers that the production of pancreatic necrosis, according to this series of experiments, depends upon three factors. (1) There must be a simultaneous and complete prevention of the escape of both pancreatic juice and bile from the duodenum. (2) The presence of infectious material in the gall-bladder. (In those cases in which the papilla were ligated but no bacteria introduced into the gall-bladder, no pancreatic necrosis ensued.) (3) Predisposing anatomical formation which is regularly present in dogs and occasionally present in some people, namely, an ending of both common bile duct and pancreatic ducts into a small ampulla just above the papilla. Here obstruction of the papilla will lead to entrance of bile into the pancreatic ducts, as shown by Opie many years ago.

In every one of Nordmann's 8 cases, cholelithiasis was demonstrated either at operation or at autopsy. Twice when the gall-bladder and common duct were drained, for a time pancreatic juice escaped from the drain lying in the common duct. From this, Nordmann deduces that both common duct and pancreatic duct must have joined one another above the papilla. He advises routine drainage of the bile passages in every case of pancreatic necrosis.

**Pancreatic Lymphangitis.** While it is conceded that the most frequent origin of pancreatic infection is direct extension of inflammation in the bile ducts, nevertheless, not enough stress has been laid upon the relatively rarer infection of the pancreas by way of the lymphatics.

Deaver,<sup>1</sup> in speaking of pancreatic lymphangitis, says, "A fact which is difficult to explain on the theory that such swellings result from duct borne infection, is the usual localization of the lesion in the head of the organ, the tail, as a rule, being unaffected so far as can be determined by palpation." Again, "the so-called triangle of pancreatic inflamma-

<sup>1</sup> Annals of Surgery, August, 1913, p. 151

tion lying between the duodenum and the converging ducts of Wirsung and Santorini should not be so commonly affected to the exclusion of the remainder of the pancreas were the infection carried by the ducts, since the remainder of the pancreatic tissue is just as truly supplied by, and dependent on, these ducts as are the tissues of the triangle. In our opinion, a more significant relation is to be found in the proximity of the common duct in its retroduodenal and pancreatic course to this portion of the head of the pancreas." He implies thereby that the path of infection is by way of the lymphatic rather than by direct extension. He says, "Considering the importance of the lymph channels, both in the transmission of infection and in recovery therefrom, this neglect is unjustifiable. The pancreas is well supplied with lymph vessels which run in the intralobular septa in company with the bloodvessels and ducts. Unlike the majority of glands, the pancreas presents no great hilum through which emerge the bloodvessels and ducts to unite into trunks of supply.

The lymphatics emerge at various points along the course of the glands and make their way through the retroperitoneal cellular tissue to join the thoracic duct. In this retroperitoneal tissue they anastomose with lymph trunks coming from the stomach, duodenum, spleen, liver, gall-bladder, and bile ducts, the colon and even the left suprarenal. Probably still other intercommunications exist which have not yet been demonstrated."

Deaver refers to the work of Bartell in demonstrating the particular intimacy between lymphatics of the duodenum and the head of the pancreas, and to the work of Franke showing a similar close relationship between the lymphatics of the gall-bladder and the head of the pancreas. He says "that gall-bladder and duodenal inflammation do cause marked peripancreatic lymphangitis is very easily made out. We have seen scores of such cases since we began to recognize the condition."

"The irregularly segmental distribution of the lymphatics of the pancreas harmonizes well with the localized areas of infection observed clinically."

Arnsperger<sup>1</sup> reports 3 cases of acute hemorrhagic pancreatitis with diffuse fat necrosis, in each of which there was a marked cholecystitis with gall-stones. The deeper bile passages, the pancreatic duct, and the duodenum were absolutely free from inflammatory changes. Arnsperger interprets these cases as infection of the pancreas by way of the lymph channels from the primarily infected gall-bladder, he also cites the fact, as proof of this, that the case in which the bile passages were drained, recovered at first and later on died at home four weeks afterward, while the other 2 cases, in which the pancreas was merely

<sup>1</sup> Deutsch. Gesellsch. f. Chir., 1913

drained, died within a few days. Arnsperger refers to his article in the *Münchener medizinische Wochenschrift* of 1911, No. 14, in which he describes production of chronic pancreatitis by lymphatic extension from the gall-bladder.

In discussing the SURGERY OF THE PANCREAS, W. J. Mayo<sup>1</sup> calls attention to the fact that the pancreas has no true capsule, but, when irritated, one quickly forms from the peritoneum and those tissues derived from the peritoneum.

The lymphatics of the pancreas are not collected in one group but follow the vascular supply.

INJURIES TO THE PANCREAS IN THE COURSE OF OPERATIONS ON THE STOMACH occurred in 8 per cent. of 448 resections of the stomach for benign and malignant disease done at the Mayo Clinic. In none of the operations was the main pancreatic duct reached. Usually only a superficial piece was removed from the surface at a point where the pancreas was adherent to the diseased stomach. Bleeding was free and was best controlled by a hemostatic suture on a curved needle. As a result of the localized peritonitis, the pancreas, in all these cases, was found enveloped in a fibrous capsule. After resections of the pylorus for carcinoma, the duodenum is closed with two superimposed purse-string sutures and then the closed duodenal stump is applied directly to the wound in the pancreas, as recommended by Willy Meyer (see remarks on Resections of the Stomach, p. 110). The anterior peritoneum and adventitious sheath of pancreas is then sutured to the anterior surface of the duodenum. The Mayos have used this method for something like six years and have not had a single leakage either from the duodenum or from the pancreas (Figs. 61 and 62).

Ulcers of the posterior wall of the stomach usually form an excavation into the body of the pancreas, and it is necessary to excise them cleanly well down into the pancreatic tissue, leaving no area of infection behind. As this opening cannot be closed by suture, hemorrhage must be controlled by hemostatic sutures. A piece of gastrohepatic or gastrocolic omentum is then mobilized and turned into the excavation in the body of the pancreas where it is held in place by catgut sutures. Experience has shown that drainage is unnecessary.

For injuries to the pancreas in the course of operations on the spleen see remarks on Splenectomy.

RESECTION OF THE PANCREAS FOR TUMOR is a very rare operation. To the 17 cases reported by Finney, the Mayos add one of their own, making 10 recoveries and 8 deaths in the series, all the fatalities occurring in cases of resection for malignant disease.

Their case was a woman, aged thirty-seven years, in whom the diagnosis was made of cholelithiasis, with pancreatic involvement. The

<sup>1</sup> Annals of Surgery, August, 1913, p. 145.

abdomen was opened through a right rectus incision near the free border. A hard, irregular tumor the size of an egg was found in the body of the pancreas about its middle, a second working incision was made through the left upper rectus, the gastrocolic omentum was divided, the stomach was drawn upward and the transverse colon downward, thus exposing the body of the pancreas and the tumor. It seemed best to begin at the tail and remove the left half of the pancreas with the tumor. Removal was very difficult on account of the deep fixation of the pancreas. Hemorrhage from one of the deep veins was extremely difficult of control on account of the risk of injury to the splenic vessels. Finally the tail and the body of the pancreas with the tumor, about four and one-half inches in all, was separated, a strong clamp was applied across the body one inch to the right of the tumor and the left half of the pancreas with the tumor was cut away. Four clamps had previously been attached to vessels in the depth of the wound. Attempts to pass hemostatic sutures resulted in fresh bleeding, and another clamp was applied to control this. All the clamps, including the one across the body of the pancreas, had their handles brought to the surface and the cavity from which the pancreas had been excavated was loosely packed with gauze. The clamps were loosened on the fourth day and removed on the fifth. The gauze was taken out on the tenth day. Recovery was uneventful. The tumor proved to be a benign, thick-walled, trabeculated cyst buried in sclerosed pancreatic tissue.

**The Accessory Pancreas; its Surgical Significance.** According to Carwardine and Short,<sup>1</sup> an accessory pancreas is probably not an excessively rare abnormality. It usually occurs as a small, rounded nodule which may be as large as a filbert, situated somewhere in the wall of the alimentary canal. Thus it has been found: (1) in the wall of the stomach, either near the pylorus or the greater or lesser curvature; (2) in the wall of the duodenum detached from the true pancreas; and (3) in the first eight inches of the jejunum, this is its commonest location; and lastly, (4) in the lower jejunum or ileum. In one case it was found close to the umbilicus in the abdominal wall.

In some cases, it has lain between the normal mucosa and the serosa. In others, the mucosa has been thinned out over it and it has passed into the lumen of the bowel. According to Rendle and Short, the accessory pancreas gives trouble in four ways:

1. It may produce mechanical alterations in the walls of the alimentary canal, especially in those cases in which pancreatic tissue has formed a complete ring around the duodenum with some narrowing (see reference to *pancreas annulaire*<sup>2</sup>).

2. The accessory pancreas is liable to acute pancreatitis. Such a case is reported by Short, in which the condition produced extreme

<sup>1</sup> Annals of Surgery, May, 1913, p. 653.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1912, p. 146.

inflammation of the wall of the surrounding jejunum and symptoms of a high acute intestinal obstruction. The first six inches of the jejunum was bright scarlet in color and the wall was more than half an inch thick, gradually shading off distally to normal jejunum. About one and one-half inches from the duodeno-jejunal flexure in the wall of the jejunum was a white nodule projecting slightly under the serous coat. It was about a half-inch in diameter and nearly escaped observation. It projected slightly into the lumen of the bowel. There was no peritonitis or lymph clots. The little nodule was excised on the supposition that it might be a sarcoma or myoma. In any case it was evidently the source of infection. The bowel was then sewed up longitudinally. Unfortunately, the wall was so thick that this narrowed the lumen to such a degree that posterior gastro-jejunostomy had to be performed of a necessity. The patient died fifty hours after operation without signs of peritonitis. No autopsy was permitted.

3. The accessory pancreas may develop chronic interstitial pancreatitis, as shown in the case reported by Mayo Robson.

4. The accessory pancreas may complicate the diagnosis of the cause of abdominal symptoms, as shown in a case of Carwardine's. An accessory pancreas the size of a filbert situated two inches from the duodeno-jejunal flexure in the wall of the jejunum was found as a complication of what in all probability was a carcinoma of the pylorus.

### THE SPLEEN.

**Blood Conditions in which Splenectomy has Proved of Value.** The indications for performing splenectomy in certain conditions of the blood are becoming more sharply defined as time goes on. Among the different investigators in this field, none is more prominent than Eppinger.<sup>1</sup> This author reports observations upon numerous cases in which splenectomy had been performed for enlarged spleen.

1. The jaundice which often accompanies enlargement of the spleen, tends to disappear after its removal. After freeing the lipoids in the blood from cholesterol, Eppinger and his assistants, King and Medak, determined that the degree of clinical hemolysis present, and the iodine index of the lipoids, paralleled one another.<sup>2</sup> It was found that the iodin index sinks after extirpation of the spleen, the fat content of the blood rises (as also shown in dogs). A very high iodin index was found in the blood lipoids of cases of pernicious anemia, cirrhosis of the liver, hemolytic icterus, and the passive congestion of cardiac insufficiency.

2. By using the spectrophotometric method of Charnass, it was ascertained that large amounts of urobilin were given off in the stools

<sup>1</sup> Berl. klin. Woeh., 1913, No. 33 and 34.

<sup>2</sup> The high iodin index indicates the presence of unsaturated fatty acids whose powerful hemolytic effect is a matter of common knowledge.

of patients suffering with pernicious anemia, hemolytic ieterus, malaria, lead poisoning, pneumonia, and the passive congestion of decompensated cardiac conditions; while low amounts were found in the cachexia of malignant disease, postpartum anemia, and similar conditions.

3. The amounts of urobilin present in the stool in pernicious anemia and hemolytic ieterus, underwent great diminution following splenectomy.

4. Splenectomy gave good results in 2 cases of Banti's disease, 2 hypertrophic cirrhosis of the liver, and 1 ieterus catarrhalis gravis, *i.e.*, catarrhal jaundice of such severity that a transition to acute yellow atrophy of the liver seemed imminent.

5. The spleens in pernicious anemia, hemolytic ieterus, and experimental toluidine-diamin poisoning, resemble one another, inasmuch as they are crowded with erythrocytes. (There seems to be a parallel between the degree of hemolysis going on in the spleen, and the quantity of blood present in it.)

Therapy should not be directed toward exaggerating the function of the red bone marrow by tonics and similar means, but should attack the hemolytic processes going on in the spleen by splenectomy.

Klemperer and Hirschfeld<sup>1</sup> arrived at the same conclusions regarding the therapeutic value of splenectomy but by a different route. In a patient of theirs whose spleen had been removed for Banti's disease, they observed the development of a polycythemia within a year and a half after the operation (red cells 7,000,000 to 8,000,000, hemoglobin over 120 per cent.). A number of cases of polycythemia have also been observed following splenectomy performed for rupture of the spleen. Splenectomy was accordingly tried in 3 cases of pernicious anemia. One died of a postoperative bronchopneumonia three days after operation; the other 2 made uneventful recoveries. There was steady improvement, both in subjective and objective symptoms. The sternal tenderness diminished, the lemon-colored hue of the skin disappeared, the urobilin diminished to an almost imperceptible quantity; the hemoglobin and red count rose. The blood picture changed for the better, although it did not lose the characteristics typical of pernicious anemia.

Immediately following extirpation of the spleen, a large number of normoblasts and erythrocytes containing Jolly bodies, appeared in the blood, as evidence of the regenerative capacity of the red bone marrow. In the authors' experience, no other measure, employed in the treatment of pernicious anemia, had ever evoked so powerful a reaction on the part of the bone marrow.

At the time of their writing, September, 1913, the addition of Klemperer and Hirschfeld's 2 cases, brought the total number of splenectomies for pernicious anemia up to 6.

<sup>1</sup> Therapie d. Gegenwart, 1913, p. 385.

At the Naturforscherversammlung, in Vienna, in the Autumn, Eppinger and Ranzi embodied their ideas in as comprehensive a paper as the indefinite character of their subject permitted. They stated that among other functions, the spleen possesses the ability to destroy red-blood cells. In health, this function remains within normal limits, while in disease it may be exaggerated to such a degree that the stability of the hemoglobin content of the blood is disturbed. They state that the only correct indicator for judging the destruction of hemoglobin, is the amount of altered biliary pigment given off. They accordingly estimated the biliary pigment in the form of urobilin in the stool, and used it as an indicator.

Their experience is summarized as follows:

In *hemolytic icterus*, splenectomy gave brilliant results. (The post-operative decrease of urobilin excretion has been mentioned above.)

Certain forms of *pernicious anemia* have a relationship with hemolytic icterus, the difference between the two being merely one of degree. The enlargement of the spleen, though slight, is often an indication that the source of the trouble lies here. However, increased destruction of the red-blood cells often goes on in a spleen of normal size. In hemolytic icterus, the blood-forming organs may compensate the destruction to a remarkable degree, whereas in pernicious anemia, the red bone marrow's function undergoes an early paralysis. Splenectomy affords the only chance the red marrow has of regaining its function. The clinical improvement is remarkable; the blood picture, however, retains its former general characteristics.

BANTI'S DISEASE. The heightened hemolytic process in the spleen may cause secondary changes in it. What Banti has described as "fibro-adenie," is held by Eppinger and Ranzi as an expression of such a chronic process, and they even suggest that this is evidence of an attempted healing. They do not agree with Banti's ideas concerning this syndrome. Here the effect of splenectomy is not as striking as with cases of hemolytic icterus. The symptoms subside very slowly.

IN HYPERTROPHIC CIRRHOSIS OF THE LIVER splenectomy has given excellent results. In the condition of pathological hemolysis, the liver is also affected. For, just as certain hemolytic poisons, such as toloulendiamin, may cause changes in the liver, so likewise may the exaggerated hemolytic processes in the spleen, cause damage to the liver. It would seem as though hypertrophic cirrhosis of the liver occurred secondarily to a primary affection of the spleen. It is conceivable that the severity of many hepatic diseases, such as alcoholic cirrhosis, depends directly upon the hemolytic function of the spleen, which latter is surely subject to individual variation. The longer the icterus has persisted, the more advanced and permanent are the changes found in the liver. In such cases one cannot expect immediate improvement following splenectomy. It may take months before the icterus finally disappears.

The last of the conditions enumerated by Eppinger and Ranzi is a PRIMARY PYLEPHILEBITIS OF THE SPLENIC VEIN. (It is not easy to follow the method by which they arrive at this diagnosis.) These cases present the picture of a sepsis in which enlargement of the spleen occurs shortly after the onset. (Plasmodia must always be looked for on account of the ease with which this condition may be confused with malaria.) Operation or autopsy invariably reveals an enormous dilatation of the splenic vein and its branches. In many cases the collaterals enlarge to the size of the little finger. Those in the wall of the stomach may rupture, giving rise to a hematemesis, or to blood in the stool. Eppinger and Ranzi interpret the condition as a primary phlebitis of the splenic vein causing passive congestion of the spleen with consequent enlargement. They advise splenectomy because of the imminent danger from rupture of the collaterals.

In the discussion which followed this paper, Exner reported 10 cases of splenectomy. Of these, there were 3 of Banti's disease, 3 of hemolytic ieterus, and 4 of pernicious anemia.

Von Haberer (1 case), Decastello (3 cases), and Mosse (1 case), all observed immediate postoperative improvement after splenectomy for pernicious anemia.

Eppinger, in closing, reported an additional case of hypertrophic cirrhosis of the liver in which a brilliant recovery followed splenectomy (performed by Brauer).

Everyone agrees that it is too early to draw definite conclusions regarding the permanent cure of these conditions, especially pernicious anemia. Here the fact that the pathognomonic blood picture persists in spite of the marked clinical improvement, makes the probability of a permanent cure very questionable. Another year or two will shed much light on the subject.

THE GAUCHER TYPE OF SPLENOMEGALY is an absolutely distinct clinical entity. The patients feel perfectly well. The fact that they possess a greatly enlarged spleen is discovered by mere chance. In most of the cases the blood picture is normal, the anemia noted in some of the cases is a coincidence and had nothing to do with the enlargement of the spleen. "The splenic enlargement is caused by proliferation of its endothelium, with a secondary connective-tissue overgrowth which is followed by a colloid degeneration of the endothelium" (Wilson). It is of interest to note that several members of the same family are often found to be affected with this condition.

In speaking of its treatment, Wilson<sup>1</sup> says: "It seems to me unfortunate that the trend of medical thought was originally directed toward the consideration of these endothelial proliferations as true neoplasm, with the associated dread of malignancy, since it has no doubt operated to prevent surgeons from hazarding splenectomy; though, of the 9 cases which have been operated upon as reported in the

<sup>1</sup> Surgery, Gynecology, and Obstetrics, March, 1913, p. 247.

literature, 4 have recovered, while the remaining 5 were in very bad condition before coming to operation." The article by Erdman and Moorhead<sup>1</sup> contains a list of ten splenectomies for Gaucher type of splenomegaly including one of their own. Of the ten, two died within a few hours after operation, the rest recovered, and, so far as is known, have remained well ever since.

**Surgery of the Spleen.** Comprehensive reviews have appeared by W. J. Mayo,<sup>2</sup> and, in German, by Michelsson.<sup>3</sup> The latter author calls attention to the slight degree of trauma necessary to cause a rupture of the spleen in such conditions as malaria or typhoid fever; it has been known to occur after sneezing, coughing, or vomiting.

Then follows a consideration of the subcutaneous injuries of the spleen which contains nothing particularly new.

Shot and stab wounds of the spleen are usually complicated by injury of other organs, such as lung, pleura, diaphragm, stomach, and intestines. Michelsson insists that isolated injuries of the normal spleen can only occur in those cases in which the diaphragm is in the position of deepest inspiration (that it has pressed the spleen down as far as possible), at the moment of injury. In stab wounds of the left chest where the diaphragm has also been perforated, Michelsson not only advises an exploratory thoracotomy but also an exploratory laparotomy. In this connection it may be of interest to note that in the Sauerbruch-Schumacher surgery of the thorax, such a gunshot injury is described. The left lower thorax was opened, the wound in the lung was sutured, and the diaphragm was split in the direction of the fibers, thus exposing the lacerated spleen which was removed by this route with more ease than is usually the case by way of the abdomen.

The sections on abscess, cysts, tumors, and wandering spleens bring the subject up to date but contain little that is new.

**THE TECHNIQUE OF SPLENECTOMY.** W. J. Mayo<sup>4</sup> says, "for the removal of a large spleen, an incision is made in the outer margin of the left rectus muscle extending from the costal arch downward until there is a space sufficient for manipulation.<sup>5</sup> For smaller spleens, a transverse incision is practicable.<sup>6</sup>

<sup>1</sup> American Journal of Medical Sciences, February, 1914, p. 213.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, March, 1913, p. 233.

<sup>3</sup> Ergebnisse d. Chir. u. Orthop., Band vi, p. 480 to 535.

<sup>4</sup> Surgery, Gynecology, and Obstetrics, March, 1913, p. 238.

<sup>5</sup> Owen: In the British Journal of Surgery, vol. i, No. 3, in reporting a series of cases of splenectomy performed in Egypt with similar incision, concedes that this cuts the nerves to the rectus and results in atrophy of the rectus, mesial to the line of incision. He states that this does no harm provided the fascia is firmly united, and he reports late results on a number of these cases in which hard manual labor in the field was being performed without the slightest inconvenience or sign of hernia.

<sup>6</sup> The combination of vertical and transverse incisions recommended by Rodman and Willard (Annals of Surgery, November 19, 1913, p. 601) is practically identical with that of Perthes (see PROGRESSIVE MEDICINE for June, 1913, p. 74, Figs. 49 and 50), although they make no reference to this author.

"On opening the abdomen, the hand is passed over the spleen under the diaphragm, and, if adhesions are present, they can usually be broken down with the hand. The spleen can now be brought entirely out of the abdominal incision. The fundus of the stomach and the colon come out with the spleen, and these attachments, together with the lienophrenic ligament, can be tied and divided under inspection.

"A large gauze pack is carried up into the cavity from which the spleen has been removed, to check the oozing from the separated adhesions. The spleen is then steadied, and all of the attachments tied and divided until it remains attached only by its vascular pedicle. A rubber-covered elastic clamp of the tower variety is placed on the pedicle, if possible, about three inches from the spleen. If portions of the stomach or colon are caught with the pedicle by the elastic holding clamp, no injury will result. This hold prevents slipping and sudden hemorrhage from the great vascular pedicle, and the vessels can be divided close to the spleen into three or four sections and ligated carefully with cat-gut, before the holding clamps are removed.

"In hypertrophied spleens of long standing, the bloodvessels are often atheromatous, necessitating great care in placing the ligature (this has also been the experience of others). After ligating the vessels, the clamps on the base of the pedicle are loosened gradually, the large gauze pack is removed and the bleeding points of the deep cavity closed with cat-gut on a fine needle." In one case, Mayo was unable to control a hemorrhage from the under surface of the diaphragm and was compelled to leave a large gauze pack in the cavity, removing it several days later.

The tail of the pancreas is sometimes drawn up with the pedicle, and, unless care be exercised, it may be accidentally tied in the pedicle and divided. In one case Mayo removed one and a half inches of the tail of the pancreas with the pedicle and did not discover it until he was about to drop the pedicle back. He covered the pancreatic stump with peritoneum and drained with a fine rubber tube through a stab wound in the side. This precaution, however, proved unnecessary, as there was no leakage. Mayo states that the operation, if the patient be in fair condition, should not have a mortality above 10 per cent., probably not above 5 per cent. There were 27 cases, with 2 operative deaths. Among these cases were 18 of splenic anemia, 5 of which showed the Banti syndrome, 1 of pernicious anemia, and 1 of cirrhosis of the liver.



## GYNECOLOGY.

BY JOHN G. CLARK, M.D.

### CANCER OF THE UTERUS.

**The Cancer Problem. Radiotherapy.** The foregoing year has been the witness of a most remarkable wave of excitement and enthusiasm—one might almost say hysteria—with regard to the possibilities of radioactive forces in the treatment of malignant processes, which has swept through both the scientific and lay worlds. Just why this tremendous interest should have burst forth at this particular time is a little difficult to say, for nothing radically new, or at least nothing that was not known in a general way to those who have been working in recent years with radio-active substances, has been brought out in the past twelve-month, and yet both the medical and lay press have been inundated with articles on the subject, the legislative bodies of municipalities, states, and nations have been aroused to appropriate large sums for the purchase of radium and the establishment of institutes for its use, and the public has been at times almost led to believe that the long fight against cancer is ended, that the millennium has arrived, and that the cure is at hand.

That much has been accomplished of real, solid worth is undoubtedly true; with increasing quantities of radium and allied substances coming into the hands of those who have acquired experience in their use, with the gradual development of a rational technique in their application, and of an understanding of their indications and contra-indications, more and more tangible results are being attained, and still greater prospects for accomplishment in the future are opening up, but that we are still an interminably long way from the true realization of a universally or even generally efficient non-surgical treatment for any but the most superficial forms of malignancy, no one would be quicker to emphasize than those who have had the greatest experience with radiotherapy. Both good and harm is likely to result from this popular dissemination of a certain amount of knowledge upon the subject; good, in that interest will be, and indeed has been, aroused in the discovery, proper conservation, and development of radium-bearing deposits, and in the establishment for public benefit of institutions equipped for the scientific application of radiotherapy; harm, in that false hopes will be aroused, and in many instances a false sense of security

stimulated, whereby the golden opportunity for efficient surgical intervention may be lost, and, finally, in that the door will be opened for many quacks and charlatans still further to defraud a gullible public. If there is any form of treatment in the world which lends itself to fraudulent imitation, it is certainly that by radium. A tiny metal tube or capsule is placed for a time in contact with the patient, who does not even see its contents, much less become aware of immediate or tangible results, and who must therefore trust absolutely to the honesty and ability of the man who is applying the treatment that a really efficient salt in suitable amounts is being used. It would seem of the utmost importance, therefore, that not only the laity, but also the profession should be emphatically warned that radiotherapy as a scientific method for the treatment of malignant disease, especially of the types interesting the gynecologist, is still in its swaddling clothes, and that comparatively small amounts of truly active radium salts exist as yet in this country, these being, moreover, in the hands of a very few men.

This wave of widespread interest in radiant energy as a therapeutic force apparently struck the continent of Europe, and especially the German Empire, several months before it reached this country; in Germany, a large, if not the major, portion of the activity displayed along this line has come from the gynecologists, and the chief subject of attack has been uterine carcinoma; in this country, on the other hand, the gynecological applications of radium have not been particularly emphasized, notwithstanding the fact that one of our leading gynecologists has been one of the earliest and most enthusiastic workers with it. The result of this is that while the medical literature of this country furnishes but few reports of the use of radium in strictly gynecological conditions, that of Germany and Austria has been, during the past year, literally teeming with such articles, so much so that only a comparatively few can be selected for consideration here.

In using the term "radiotherapy," we include the therapeutic action of all forms of radiant energy, whether this be derived from chemical substances, such as radium, mesothorium, etc., or from the *x*-ray tube, and indeed most of the experimenters in the field have worked with both these sources of energy, as will be seen by reference to the reports quoted below. There is apparently a certain amount of question in the scientific world as to the identity or non-identity, physically and therapeutically, of certain of the groups of rays obtainable from radioactive chemical substances and from the Röntgen tube, and consequently as to their interchangeability for therapeutic purposes. Some authors, such as Pagenstecher,<sup>1</sup> for instance, believe that the hardest rays given off by a Röntgen apparatus are practically identical with the  $\gamma$ -rays of radium; the majority of investigators do not appear to agree with

<sup>1</sup> Münch. med. Wochenschr., 1913, vol. lx, p. 2562.

this view, however, but hold that the  $\gamma$ -rays obtained from radium preparations possess qualities of penetrability and destructiveness which cannot be equalled by any form of emanations from the  $x$ -ray tube. The almost prohibitive price of radium itself has been a stimulation, however, to the attempt to discover some method or substance by means of which results comparable to those produced by it may be obtained at a less cost. The most important of the various substances which have been tried for this purpose is *mesothorium*, a material which has aroused, in Germany at least, almost as much popular and scientific interest as radium itself. Reference to this substance was made in these pages last year; it is a by-product in the manufacture of incandescent gas-mantles, being derived from a mineral occurring chiefly in Brazil, "monazitsand." Physically, it is the first degeneration product of thorium, and as regularly prepared, contains 25 per cent. of true radium. Its radio-activity increases until the maximum is reached about three years after its manufacture; it then begins to weaken, and in twenty years falls to half the maximum activity; finally, when all of the mesothorium has degenerated, the only energy left being due to the 25 per cent. of radium, which loses only one-half its power in 1800 years. The chief difference of action between mesothorium and pure radium is that the former sends off a larger proportion of the soft  $\alpha$ - and  $\beta$ -rays, and a correspondingly smaller proportion of the hard  $\gamma$ -rays than does the latter.<sup>1</sup>

The following reports of investigations with radiotherapy in uterine and allied carcinomata have been chosen as presenting for the most part the work of men whose extensive experience with older methods of treatment permits them to speak authoritatively with regard to the value of the new. Care has been taken to give, wherever possible, sufficient details of the technique employed to furnish some ground for a rational comparison of the efficiency of various methods. The two points of technique which appear to be of the greatest moment, whether one be working with  $x$ -rays, radium, or mesothorium, are the amount of *filtration* applied to eliminate the softer rays, and the *dosage*. In expressing the latter factor, as related to the  $x$ -rays, all dosages given have been reduced to the so-called Kienbock " $x$ -unit," 100 such units, for instance, being expressed by the term "100-X." The dosage of radioactive substances, such as radium or mesothorium, is uniformly expressed in terms of "milligram-hours," representing the amount of the substance in milligrams times the number of hours over which it is allowed to act; thus, 10 milligrams of radium, applied to a tumor for five hours, would give a dosage of 50 milligram-hours.

MESOTHOРИUM TREATMENT AT FREIBURG. Krönig and Gauss, who are, as is well known, the most ardent advocates today of the  $x$ -ray

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1913, p. 193; Wanner and Teutschlaender, Monatssehr. f. Geb. u. Gyn., 1913, vol. xxxviii, p. 296.

treatment of uterine myomas and metropathias, and whose work along these lines has been previously discussed at length in these pages,<sup>1</sup> report in a recent paper<sup>2</sup> their results so far in the treatment of malignant conditions with *mesothorium*. In this work they have adopted the same general principles which have given them such brilliant results with the *x*-rays, namely, the use of *very large doses*, applied in concentrated form, close to the tissue to be affected, a *high degree of filtration*, to exclude all but the hardest and most penetrating rays, and the utilization of the principle of "*cross-fire*," *i. e.*, the application of the rays from numerous portals of entry. In the treatment of cancer, *e. g.*, they have used as much as 800 milligrams of mesothorium at one application.

In order completely to cut off the  $\alpha$ - and  $\beta$ -rays, Krönig and Gauss have not found aluminum filters, such as they use in *x*-ray work, sufficient, and they have therefore used lead quite extensively, but in situations where the container must be of comparatively small size, gold and platinum have been substituted. As a general rule, a thickness of 0.5 mm. of platinum, 1 mm. of gold, or 2 mm. to 3 mm. of lead has been found the most efficient. The necessity for using large amounts of material is due primarily to the fact that the  $\gamma$ -rays, which alone are of service in treating anything but the most superficial cancers, and which alone penetrate any of the above described filter-capsules, compose an extremely small portion (less than 1 per cent.) of the total radiant energy of mesothorium, over 99 per cent. of its emanations being cut off by the filter.

Still another factor is of great importance—the time of exposure. In accordance with the authors' general principle of dosage to the limit of endurance, they have endeavored to determine the biological tolerance of tissues to the  $\gamma$ -radiations, and have found that even the above mentioned enormous quantities of radio-active substances can be left *in situ* for as long as eight days at a time, provided proper precautions are taken.

The experiments of the authors in the radiotherapy of carcinoma cover in all 146 cases. Of these, 26 were unoperated patients, subjected to unfiltered or weakly filtered rays; the results obtained were similar to those reported by numerous investigators—cessation of hemorrhage, superficial cicatrization, and increase in the mobility of the tumor. In no case was a cure produced, however, and so far as known all these patients eventually died from the malignant process.

Irradiation to prevent recurrence after operation was done in 64 cases; in some with unfiltered, in others, more recently, with filtered rays. Of 43 cases belonging to the first group, 20 are known to have died of carcinoma, while the fate of the others is unknown; of the 21 patients forming the second group, 30 are known to be alive and free

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1912, p. 192; and June, 1913, p. 224.

<sup>2</sup> Deut. med. Wochenschr., 1913, vol. xxix, p. 1233.

from recurrence, and the fate of 1 is unknown. While, of course, some of these latter are comparatively recent cases, and have been under observation but a short time, 13 of them have been followed for over a year and a half—of these, 1 for over five years; 2 for over four years; and 1 for over three years.

Of unoperated cases treated with filtered rays, there were 56; many of these received both *x*-ray exposures and mesothorium applications, this combined treatment being the method which Krönig and Gauss believe holds out the greatest hope. Five of these patients have died, 7 have disappeared, and 26 are apparently cured, *i. e.*, they are in perfect health, free from all symptoms, and deep excisions of tissue fail to reveal the presence of any carcinoma. The longest period of freedom from recurrence as yet is but one year and nine months, however.

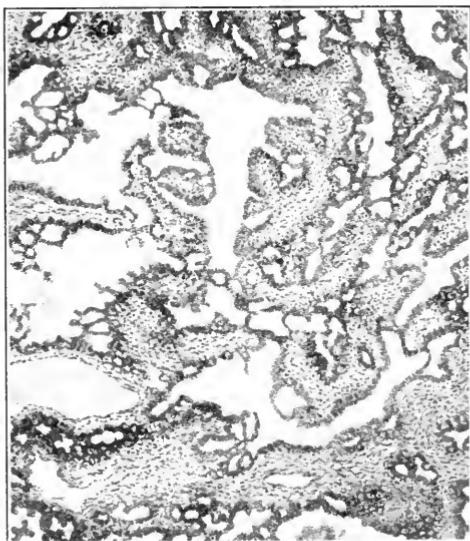


FIG. 87

In view of the excellent results obtained with radiotherapy when the growth is not too hopelessly advanced, the authors advocate a somewhat more radical stand-point than is taken by the majority of men today, namely, to extend the indications for radiotherapy to include some cases of still operable tumors, such, *e. g.*, as early carcinoma corporis uteri, which in its beginning is generally a surface growth. If after a two to three weeks' trial with radiotherapy no appreciable effect is produced, then they would advise operation, believing that not only will sufficient time to reduce the chances of a successful operation not have been lost, but that these chances will be improved, as many of the outlying malignant elements will have been destroyed.

In another paper, Gauss<sup>1</sup> reviews from the pathological stand-point 30 cases of uterine carcinoma which have been treated in the Freiberg Clinic with mesothorium. So far as can be told as yet, 10 of these patients appear to be clinically cured, and the histological examination of bits of tissue excised from time to time during the course of treatment revealed such striking changes as in some instances almost to lead to a suspicion of a mixing of the specimens. Fig. 87, for instance, shows a bit of tissue from an adenocarcinoma of the uterus at the beginning of treatment; Fig. 88 gives the appearance two weeks later, showing a great proliferation of the fibrous connective tissue surrounding the sparsely scattered cancer nests, while in material removed by curettage three weeks after commencing treatment nothing was present but

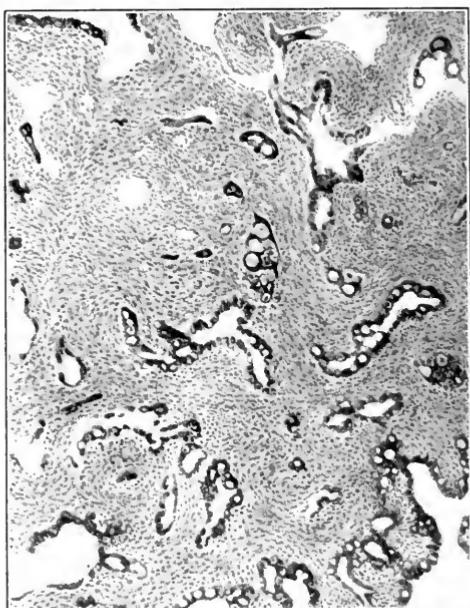


FIG. 88

benign tissue and some epithelial debris (Fig. 89). Gauss admits that as yet the technique of radiotherapy by the use of substances such as radium and mesothorium is not nearly so perfected as is that of the  $x$ -ray, but he thinks that it soon will be, and that this form of treatment has a great future in gynecology.

*Importance of Large Doses.* Pinkuss<sup>2</sup> also emphasizes the importance of employing adequate filters in working with mesothorium, and says that since using them he has gotten much better results than

<sup>1</sup> Strahlentherapie, 1913, vol. ii, p. 623.

<sup>2</sup> Deut. med. Wochenschr., 1913, vol. ix, p. 1720.

formerly. He uses, as a rule, the  $\gamma$ -rays alone, though in some instances, in the earlier treatments, not all the  $\beta$ -rays are filtered out, the later applications consisting of pure  $\gamma$ -rays, however. Large doses are necessary, and unfortunately the supply of material is very limited; he believes that if mesothorium is to be employed at all, not less than 200 mg. should be used. The technique is still very undeveloped, and no definite method has been determined to be the best. He therefore strongly advises all patients with any carcinomatous growth which is in condition for radical operation to be operated upon, and then to have mesothorium applied, in the hope of preventing recurrence, for this purpose such large doses not being required. One serious danger of attempting to replace operation by radiotherapy, which Pinkuss brings out, is that during the lengthy course of treatment required, time may be given for

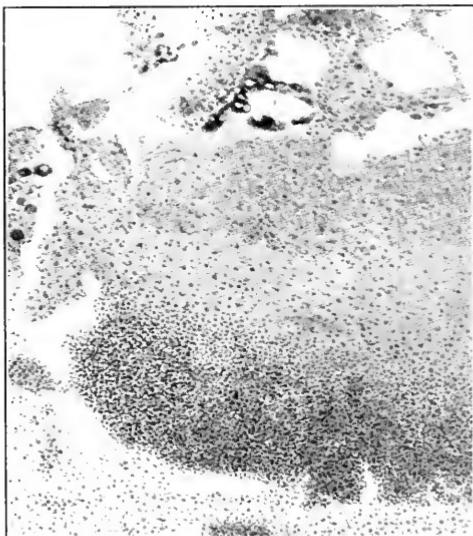


FIG. 89

metastases to occur in distant organs, even though the original growth be eventually entirely destroyed. He says that in addition to the local application of mesothorium, he has been trying in some cases the administration by mouth of thorium-X in solution, and thinks he has seen some benefit therefrom.

**COMBINED RÖNTGEN AND MESOTHORIUM TREATMENT IN MUNICH.** Döderlein<sup>1</sup> has tried the effects of both the  $x$ -ray and mesothorium in the treatment of cervical carcinoma. In giving  $x$ -ray treatments, he prefers the vaginal to the abdominal route, and projects the rays through a lead glass speculum, with the patient in the lithotomy posture. He uses an aluminum filter 3 mm. thick, and gives as large a dose as can

<sup>1</sup> Monatsschr. f. Geb. u. Gyn., 1913, vol. xxxvii, p. 553.

be furnished by the apparatus during the time the patient can remain in the necessary position, for since everything, except the actual carcinomatous tissue itself, is protected from the rays, there is no danger of injury. In addition, Döderlein has recently had placed at his disposal about 100 grams of mesothorium in 5 or 6 capsules, each covered with a sheet of silver, 0.05 mm. thick. He has been using these for direct application in the carcinomatous crater, and reports exceedingly favorable results in 6 cases.

In one instance an extensive, ulcerating, hopelessly inoperable carcinoma was reduced in about two months to a condition of operability; the uterus was extirpated, and showed, microscopically, no carcinoma whatever in the cervix, in which region the tissue was extremely hard and dense, but in the parametrium there were carcinoma cells showing apparently no destruction whatever. In the other 5 cases, all inoperable, not only was the subjective condition of the patients immensely improved, but successive excisions of bits of tissue showed microscopically a gradual necrosis, and complete disappearance of the carcinoma cells, with a corresponding new formation of connective tissue. It seems as though the latter takes on new life when relieved from the influence of the metabolic products from the carcinoma cells. Döderlein is firmly of the opinion that the destruction of the carcinoma cells is primary, and the connective-tissue growth secondary, not *vice versa*. In four very advanced cases, with extensive carcinomatous infiltration, no appreciable effect was produced. Whether larger doses of mesothorium would have been of benefit in these can be told only after further investigation, he thinks.

Sigwart<sup>1</sup> reports the case of a woman, aged thirty-four years, who had an advanced, inoperable carcinoma of the cervix, accompanied by an extensive bullous edema involving the base of the bladder, and extending well beyond the limits of the trigone. In the course of three weeks the patient was given 16,800 mg. hours of mesothorium, and an  $\alpha$ -ray exposure of 600-X. At the end of this time, the cervical tumor had become distinctly reduced in size, and was more movable, while cystoscopic examination showed a marked reduction in the extent and severity of the edema. Three weeks later, no further treatment being given, the uterus was freely movable, the cervix was practically normal in form, and the bladder mucosa showed only slight unevenness and a slight degree of hyperemia. Since the occurrence of bullous edema in carcinoma always indicates a well-advanced condition, its disappearance, Sigwart thinks, surely indicates a marked retrogression of the cancer. No information is given as to the subsequent course of the case, however.

TISSUE CHANGES FOLLOWING EXPOSURE TO MESOTHIORIUM. Wanner and Tentschlaender<sup>2</sup> report the results of careful clinical and pathological

<sup>1</sup> Zentralbl. f. Gyn., 1913, vol. xxxvii, p. 1645.

<sup>2</sup> Monatsschr. f. Geb. u. Gyn., 1913, vol. xxxviii, p. 295.

studies of a few cases of malignant disease treated with mesothorium. One patient, aged fifty-five years, was suffering from tubal carcinoma, with a cystic metastasis in the rectovaginal septum. The tube was removed by laparotomy, but the cyst could only be opened and drained from below; from its internal wall there was at first a foul discharge, containing many whitish bits of tissue. The patient was in a very bad condition, and showed the effects of toxic absorption. Treatment was soon begun by inserting into the cyst cavity 30 mg. of mesothorium in a silver capsule 0.05 mm. thick, at first for four, then for eight, twelve, and more hours at a time, in the course of seven weeks about 13,840 mg. hours being applied. During this treatment the patient's condition greatly improved; she gained in weight, and the cyst cavity closed, leaving a mass of indurated tissue in the rectovaginal septum. Microscopically the tube showed a typical cylindrical-cell carcinoma. Unfortunately, tissue from the cyst was excised for the first time only after considerable exposure to the action of mesothorium; bits were then curetted or excised at intervals. The earlier examinations showed extensive carcinomatous areas in this tissue, but these presented quite a different appearance from the primary tumor in the tube, a difference which the authors believe to be due to the action of the mesothorium rays. The epithelium in these sections showed marked degenerative changes, exactly similar to those which have been described by Döderlein and others—increase in the size of the cells, with loss of their characteristic form, increase in size of the nuclei, with marked diminution in distinctness of nuclear structure, vacuolation, and formation of detritus in the nuclei and cytoplasm. The cells give the impression of having lost the power of regeneration—they apparently increase in size, and coalesce into formless masses, but the large, chromatin-rich nuclei no longer divide, and therefore the cells finally perish. Surrounding these degenerating areas there is always a zone of active leukocytosis, the carcinomatous detritus thus finally being disposed of by phagocytic action, and the empty spaces left gradually filled by firm fibrous tissue. The chief actions of mesothorium on carcinoma would seem, therefore, to be inhibition of karyokinesis, and activation of the leukocytes. The last bit of tissue examined in this case, removed toward the end of the treatment, showed no carcinoma whatever, but merely the terminal changes noted above.

A case of advanced, ulcerating cervical carcinoma in a woman, aged sixty-two years, was treated by the same authors with 52 mg. of mesothorium, applied for twenty-four hours at a time, a total of 11,268 mg. hours being given in a little over two weeks, with resulting shrinkage and induration of the tumor, disappearance of the hemorrhage and foul discharge, and subjective improvement. A bit of tissue, curetted from the cervix two weeks after the cessation of treatment, showed only connective tissue, with intense leukocytic infiltration, but no carcinoma.

In a third case, however, a woman, aged fifty-six years, with a bilateral ovarian carcinoma and general peritoneal carcinomatosis, no beneficial effect was seen from mesothorium treatment.

Haendly<sup>1</sup> emphasizes that in order properly to judge of the histological changes produced in malignant tissue by radiotherapy, not merely bits removed from time to time by superficial excision should be examined, but that entire organs which have been subjected to irradiation must be studied, as only in this way can the changes in the deeper tissues—which form really the crux of the situation—be determined. He reports the results of detailed study of the changes in three uteri removed in Bumm's clinic, and in two obtained at autopsy, following extensive treatments with the  $\alpha$ -rays and mesothorium. Studies of this type are not numerous, but are of much importance in the determination of the much-mooted question as to just how much action in the deeper tissue we may expect from radiotherapy, and the cases are therefore reviewed more or less in detail.

CASE I.—This patient, aged forty-five years, had an inoperable cervical carcinoma, extending into the vagina and parametrium. After Röntgen treatment for five months (total dosage of 1600-X) the condition was considered operable, and the uterus was removed.<sup>2</sup> On histological examination, the cervix showed extensive large alveolar carcinoma, of the squamous-cell type, the carcinoma cells being everywhere well-preserved, and containing numerous mitotic figures. The surrounding cervical tissue was very sclerotic, very few nuclei being found in the dense, fibrous tissue, but even in this, scattered carcinoma cells were to be seen here and there. In this case the microscopic findings were in a sense disappointing, in that they were to a certain extent in marked contrast to the marked clinical improvement which had occurred.

CASE II.—A woman, aged thirty-five years. Microscopic examination of a piece of tissue excised from the cervix on admission to the clinic showed an alveolar carcinoma, with a moderate number of karyokinetic figures, and many somewhat engorged bloodvessels. The patient was treated with mesothorium, receiving within fourteen days a dosage of 9350 mg. hours, applied per vaginam, through a filter of 0.1 mm. silver and 1 mm. lead. At the end of this time a funnel-shaped, smooth-walled, clean cavity had formed in place of the ulcerated and necrotic carcinomatous tissue; operation was then performed without difficulty. Microscopically, extensive carcinomatous tissue was found in the cervix, but this showed in large part advanced degenerative changes; in the deeper portions, however, were many well-preserved and apparently still active groups of carcinoma cells. The connective-tissue fibrils showed sclerosis and hyaline degeneration; the vessels, in places, a

<sup>1</sup> Arch. f. Gyn., 1913, vol. c, p. 49.

<sup>2</sup> This case was previously reported from the clinical stand-point by Bumm himself, PROGRESSIVE MEDICINE, June, 1913, p. 195.

thickening of the intima and sclerosis of the adventitia. No effect of the treatment could be seen on metastases in a packet of lymph glands which were removed from the bifurcation of the right iliac vessels.

CASE III.—A woman, aged fifty-seven years, who had an alveolar squamous-cell carcinoma of the cervix. She was treated for three weeks with mesothorium in the same manner as the preceding case, receiving a total dosage of 13,320 mg. hours. The same gross changes in the carcinomatous crater occurred here also, and operation offered no special difficulty. Microscopic examination in this instance showed very marked degenerative changes in the carcinoma cells, from which it may be deduced that they must have been much reduced in vitality; indeed, well-preserved cancer elements were hardly to be found anywhere. In addition to sclerosis of the connective-tissue fibers, an extensive new formation of fibrous tissue had evidently taken place.

CASE IV.—A woman, aged seventy-six years, with a carcinoma of the cervix, which was inoperable on account of the extent of growth, combined with the age and poor general condition of the patient. She was treated with both *x*-rays and mesothorium, receiving a total dosage of 3880-X, and 29,075 mg. hours. At first the clinical picture improved, the tumor shrinking and drying up on the surface, with marked diminution of hemorrhage and discharge. The deep growth was not affected, however, and soon the bladder became extensively involved, the patient finally dying after four and a half months of treatment. Microscopic examination of the tissue removed at autopsy showed complete disappearance of the carcinoma at the original site, but this destruction was accompanied by a necrosis of all other tissue elements as well, this necrosis involving not only the primarily attacked portions of the cervix and vagina, but also the entire posterior bladder wall. No effect whatever was seen on a metastasis which had occurred, evidently late, in one kidney.

CASE V.—A woman, aged thirty-seven years, with carcinoma of the vagina. She had been previously operated on elsewhere, but the nature of this operation could not be ascertained. On admission, the entire posterior half of the vagina was occupied by a crater-like ulceration, with a firm, but easily bleeding wall; the lumen was so much reduced that a finger tip could barely be inserted. The patient was first treated for five days with *x*-rays, then exclusively with mesothorium, receiving a total dosage of 370-X, and 28,260 mg. hours, all applied per vaginam. Here, again, a primary clinical improvement, both subjective and objective, was noted, but several severe hemorrhages occurred from the right side of the cavity, as a result of which the patient died after about five months of treatment.

Microscopic study showed here that, under the influence of the mesothorium, such an extensive necrosis of the carcinomatous tissue had occurred that nothing whatever of the original tumor masses was to be

found. In the surrounding tissue, however, although there were no entirely healthy carcinoma cells, small nests persisted here and there, consisting of degenerating elements surrounded by detritus; the tissue surrounding these nests showed the same amount of degeneration as did the carcinoma cells themselves.

These cases all show that, with the particular technique used, practically no destructive effect, or at least no such effect of sufficient strength to accomplish the desired results, was obtained except in the *superficial portions of the growth immediately accessible to the irradiation*, and that even here this effect was accompanied by extensive destruction of the non-cancerous tissue as well, though it may be that the coincident infection, and not solely the irradiation, was in part responsible for this. Haendly believes, however, that by improvements in technique, and especially by more thorough filtration, the limitations of this form of treatment will in future be greatly reduced. The article is accompanied by several excellent microscopic drawings in color, showing the tissue changes described.

USE OF RADIOTHERAPY AT BUMM'S CLINIC IN BERLIN. Bumm and Voigt<sup>1</sup> emphasize the fact that in order to treat malignant disease successfully by radiotherapy, the diseased tissue must be well exposed to the rays. In treating uterine cancer, the operator must ascertain by careful use of the speculum the best method for exposing the tissue. If necessary, the cervix should be dilated, a contracted vagina, such as is frequently found in old women, enlarged by lateral incisions, and in the case of large growths, incisions even made into the tumor mass itself. One of the authors' cases, for instance, an advanced vulvar carcinoma, which had extended out into both inguinal regions, was treated by making a deep longitudinal incision which split the mass in two.

While radium and mesothorium have the advantage that they may be permitted to exert their effects over long periods of time without interfering with the ordinary activities of the patient, their high cost limits their use as compared with the *x-ray*, by which latter agent Bumm and Voigt believe just as good results can be obtained. They have seen, *e. g.*, two cases of urethral carcinoma, one involving the bladder, completely cured after a dosage of 700-X to 800-X had been applied. In another instance, a bit of tissue excised from a squamous-epithelial carcinoma of the cervix, after exposure to a series of *x-ray* treatments covering twenty-five days (total dosage of 664-X, applied per vaginam), showed extensive disintegration and destruction of practically all the carcinoma nests.

Although the effect of the *x-ray* is slower and weaker than that of radium or mesothorium, the result produced is the same—first an inflammatory reaction, with congestion, swelling, tenderness, and

<sup>1</sup> Münch. med. Wochenschr., 1913, vol. ix, p. 1697

increased serous discharge; in one to two weeks, however, these disappear, followed by shrinkage of the tissue, cleaning up of the surface, and fibrosis. Bumm and Voigt have been working largely with the vaginal method of applying *x*-rays to cases of cervical carcinoma, and consider that this route has great advantages, because the vagina can bear much larger doses than can the external skin. By using an aluminum filter 1 to 2 mm. thick, a dosage of 20-X to 30-X can be given daily for weeks without harm, but great care must be taken to protect the external genitalia. To provide for the patient's comfort during the comparatively long exposures necessary, the authors use a leg rest which supports the thigh, knee, and calf; by the use of this apparatus the women can remain with ease for as long as an hour at a time in the lithotomy posture, with

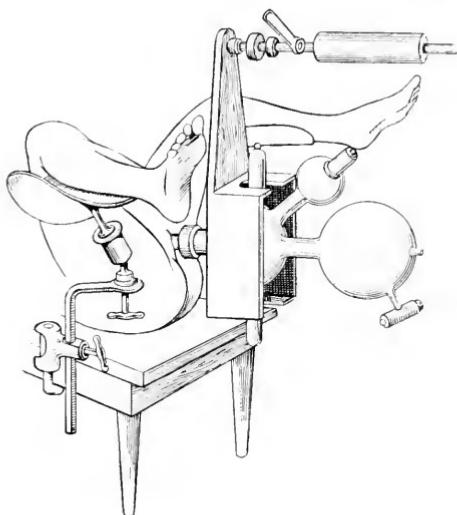


FIG. 90

a lead-glass peculum in the vagina, the *x*-ray tube being placed immediately against the outer end of this (Fig. 90). In the Bumm clinic, a large apparatus is used, which furnishes current to 4 tubes; thus 4 patients can be constantly treated side by side, one hour being allowed for each treatment, and from 24 to 30 patients are easily taken care of in a day. The authors are now attempting to develop a form of *x*-ray tube which can itself be introduced directly into the vagina, and so bring the anode into greater proximity to the carcinomatous tissue than has heretofore been possible. One difficulty encountered in this vaginal treatment, however, is the gradual shrinkage of the vagina; this has to be combated by the use of tampons and dilators.

With regard to the use of radium and mesothorium, Bumm and Voigt say that much experimentation was necessary in order to discover the correct dosage, time of application, and amount of filtration required

to produce the best results with the least irritation. They have finally come to the conclusion that doses of 150 to 300 mg. of mesothorium, allowed to work for ten to twelve hours at a time, with intervals of one to two days, best fulfil these conditions. In the majority of their cases, the two methods of treatment were combined, a Röntgen-ray sitting of one hour a day being given alternately with the mesothorium application. In order to prevent burns, they have found it necessary to place filters of at least 2 mm. of lead between the mesothorium capsule and all healthy tissue, though to produce the greatest effect upon the carcinoma the unfiltered rays should be used. They have therefore devised a simple bit-of apparatus (Fig. 91), consisting of a capsule containing 50 to 100 mg. of mesothorium, which is inserted into the carcinomatous crater, the rays being cut off above, *i. e.*, toward the corpus, by a thick lead cap. In addition to this, 100 to 200 mg. of radio-active salt are placed in a lead cup, which lies directly against the cervical lips, and prevents any rays from passing downward. The necessary lead tubes, caps, and cups must be adapted to each individual case, a matter, however, of no great difficulty.

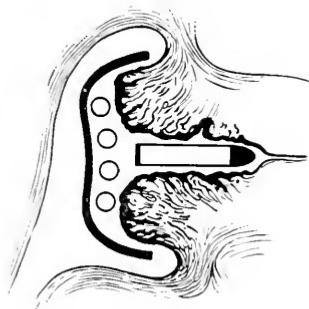


FIG. 91

Bumm and Voigt report that by the use of this combined method they have, in 13 cases of carcinoma of the uterus, and in 4 cases of carcinoma of the vulva and vagina, attained an apparent cure—*i. e.*, a complete transformation of carcinomatous into scar tissue, with complete absence of carcinoma in the pieces excised for microscopic examination. The average time covered by the treatment was fifty-five days (longest, 84; shortest, 19 days). The average total dosage of mesothorium was 14,690 mg. hours. In none of these cases, however, had more than a half-year elapsed since stopping treatment, but up to the time of presenting the report there had been no signs of recurrence.

The dangers to healthy tissue that may accompany the use of insufficiently filtered rays are commented upon in another paper by Bumm.<sup>1</sup> When using quantities of mesothorium as small as 50 mg. or less, contained in silver tubes 0.06 mm. thick, which were placed uncovered, or

<sup>1</sup> Zentralbl. f. Gyn., 1913, vol. xxxvii, p. 1236.

wrapped in an adrenalin-soaked tampon, in the cervical canal or vaginal vault for from three to twenty-four hours, Bumm experienced in four patients a superficial necrosis of the vaginal vault, which was very slow to heal. In another instance, after only two twenty-four hour treatments with 20 mg. of mesothorium, an abscess occurred in Douglas' pouch; it contained sterile pus, and eventually healed with the formation of a considerable area of induration. Although in most cases much larger doses than the above were borne without ill effect, the fact that such undesirable consequences can occur should serve as a warning not to proceed too rapidly in the administration of massive doses of radiant energy until its effects are a little better understood, and the technique of its application is a little more thoroughly worked out, than is the case at present.

TECHNIQUE OF RADIUM AND MESOTHIORIUM APPLICATION. Braude<sup>1</sup> thinks it important that the tube containing radium or mesothorium should be placed in as close proximity to the carcinomatous tissue as possible, so that the full effect of the rays may be exerted on it, without having to pass first through healthy tissue. When the tube is practically in contact with the carcinomatous tissue, many of the softer  $\beta$ -rays can be used to advantage with the  $\gamma$ -rays, whereas if healthy tissue must be traversed, practically all the former must be filtered out, thus greatly reducing the available dosage. Braude uses silver or brass tubes 25 mm. long, and about 4 mm. in diameter, varying in thickness from 0.3 to 1 mm. He does not surround them with rubber to absorb the secondary rays given off from the filter itself, as these are of no harm when they strike only malignant tissue. These tubes are introduced directly into the cervical canal until the malignant tissue immediately surrounding this has largely disappeared, and therefore forms only a thin protecting sheet between the radium tube and the surrounding structures, especially the bladder and rectum. When this stage has been reached, it becomes necessary to filter the rays more strongly, and to surround the metal capsule with rubber tissue to cut off the secondary rays. This usually necessitates placing the tube merely in the vagina, as the diameter of the package becomes too great for introduction into the cervical canal; great care must therefore be exercised not to cause any injury to the vaginal walls, which might lead to subsequent stricture or perforation. In order to shut off all the soft  $\beta$ -rays, all secondary rays, and as many as possible of the hard  $\gamma$ -rays from the vaginal walls, and at the same time to allow the full radiation to be exerted against the carcinomatous cervix, Braude has constructed a conical metal cup to fit into a modified form of the hard-rubber ring pessary (Fig. 92). This cup, which contains the radium tube, is made of lead, brass, or a combination of both; it is about 4 mm. in thickness, and is so formed that it will fit pessaries of

<sup>1</sup> Zentralbl. f. Gyn., 1914, vol. xxxviii, p. 69.

various sizes. When the metal cup and radium tube are in place in the pessary (Fig. 93), a rubber cap is drawn over the latter to hold the entire apparatus together (Fig. 94), and the pessary is then introduced in such

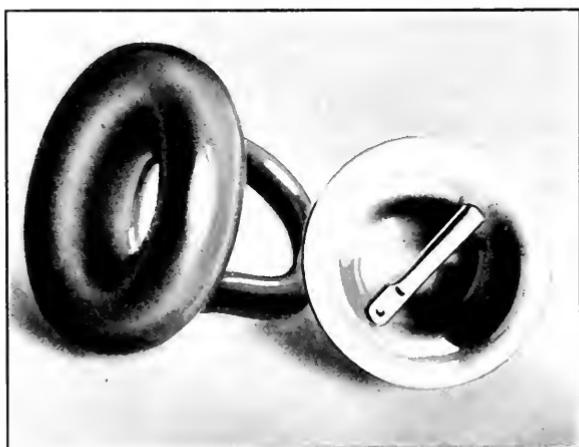


FIG. 92.—Conical metal cup to hold radium tube and fit into hard-rubber ring pessary.

a manner that the radium tube is brought into immediate contact with the cervix. A suitable-sized pessary is selected to remain firmly in position without turning or slipping; the radium container is thus kept in



FIG. 93.—Radium tube, cup, and pessary assembled.

direct contact with the carcinomatous tissue of the cervix, while the metal cup effectively protects the vaginal walls from any action of the rays.

In the application of mesothorium to uterine carcinomas, Weidner<sup>1</sup>

<sup>1</sup> Ther. d. Gegenw., 1913, vol. liv, p. 149.

has evolved a somewhat different technique. He employs a hard-rubber sound, to the end of which an aluminum capsule 0.2 mm. in thickness is firmly fixed. In this he places a quantity of mesothorium equivalent in activity to 30 mg. of pure radium bromide. The capsule is covered with sheet rubber, and wrapped in three thicknesses of gauze; it is then introduced into the vagina by means of the sound to the desired depth, and allowed to remain one to three hours, this process being repeated every day for two weeks. After an interval of from one to two weeks, a second treatment series is given, followed by another interval, and so on as long as seems necessary. With this technique Weidner has had, so far as he can tell at present, one brilliant cure, in a woman aged seventy-four years, with a very advanced, inoperable carcinoma of the cervix; for the most part, however, he has been disappointed in the results obtained, and thinks that there must be great differences in different carcinomas with respect to their radiosensitivity.



FIG. 94.—Rubber cap in place to hold parts together.

REPORTS FROM VIENNA ON THE USE OF RADIUM. Schauta<sup>1</sup> is not a strong advocate of mesothorium, and says that he thinks radium is two or three times as active as an equal quantity of mesothorium, so that since acquiring a comparatively large amount of the former, he has given up the use of mesothorium altogether. He has used both in varying doses, starting with very small amounts—10 to 25 mg.—gradually increasing these to very large doses, applied over considerable periods of time. The sole effect of the small doses was to produce sloughing and necrosis, but no curative effect whatsoever. At first he feared to use very large doses, and with increasing the dosage he did indeed encounter severe local and general reactions, but now he does not hesitate to apply as much as 100 mg. of radium, leaving this in place

<sup>1</sup> Monatsschr. f. Geb. u. Gyn., 1913, vol. xxxviii, p. 503

continually for eight days, then allowing an interval of about twice this time before reapplying it. He thinks that, as a general rule, however, such intensive doses are not well borne, and that for the average case, 40 to 50 mg. of radium, applied for five days at a time for three applications, with an interval of ten days between, is sufficient, but emphasizes that no set scheme can, as yet, be formulated; each case must be treated *individually* according to the special indications.

The changes noted by Schauta following the use of radium in carcinoma of the cervix he describes as follows: "The nodular masses covering the cervix disappear; one may almost say that they melt away as ice before the sun. The rigid, resistant, easily bleeding walls become soft and smooth; in many cases the formerly unrecognizable portio vaginalis assumes again its original contour. A distinctly *elective action* is noticeable in all these changes; in no instance was the vagina in any way inflamed; there was no necrosis produced, not even a reddening or desquamation of the epithelium could be noticed. At the end of the treatment the line of transition from carcinomatous tissue to healthy vaginal wall is generally marked by a circular wall of connective tissue in which no carcinoma is to be found, a more or less well-marked crater indicating the site of the former cancerous growth. Microscopic examination of the excised bits of tissue showed, often after the first or second application, at the latest after the third, no unaltered carcinoma, but only swollen, degenerated carcinoma cells, or none at all."

In addition to these local effects, however, Schauta encountered quite marked general reactions, such as headache, loss of appetite, gastralgia, enteralgia, alternating constipation and diarrhea, pain in the bladder region, and temperature elevation. Except in a few very cachectic and seriously ill patients, these symptoms always disappeared within twenty-four hours after removing the radium tube, and no permanent injury could be demonstrated. In a few instances quite severe hemorrhages occurred, probably as the result of destruction of tissue by the action of the radium.

In one case a vesicovaginal fistula, and in another a rectovaginal fistula resulted. This was probably due, not to any destruction of healthy tissue by the radium, but to the fact that the septa in question were completely infiltrated with carcinoma; as this was destroyed by the radium, naturally a fistula resulted.

With regard to indications, Schauta considers every case of carcinoma suitable for radiotherapy; for the present, however, he will continue to operate on all operable ones, as permanency of the apparent radium cures is not as yet determined; after operation, however, he will routinely apply moderate doses of radium to ward off recurrences. The radium is applied in capsules, covered with sheet lead or silver to filter out the softer rays. The number of cases treated so far is small, and the report, therefore, can be considered only a preliminary record of results to date.

Peham<sup>1</sup> reports the complete disappearance of a carcinoma of the clitoris, the size of a small apple, under radium treatment, leaving only smooth scar tissue; in another instance, a superficial carcinoma of the perineum was also very favorably influenced. Three cases of recurrence after radical operation for carcinoma of the cervix likewise showed beneficial results, as did seven unoperated cases of the same condition. In one of the latter, the uterus was extirpated after the application of 6000 mg. hours of radium treatment. Microscopic examination showed complete destruction of the carcinomatous tissue in the neighborhood of the surface epithelium of the portio vaginalis and cervical canal, but deeper in the tissue the destruction was less marked, and in the deepest portions practically unchanged carcinoma tissue was found, showing a distinct limitation to the penetrating power of the radium. In two instances the radiotherapy was followed by rather severe intestinal symptoms—tenesmus, discharge of mucus and pseudomembrane—and in one case by symptoms of myocarditis, which became so threatening as to force cessation of treatment. In giving these treatments, Peham used 32 mg. of radium in a platinum capsule, 0.28 mm. thick, surrounded by 2 mm. of sheet lead.

Exner<sup>2</sup> reports having used radium for ten years in the treatment of malignant tumors, with splendid results as far as superficial growths are concerned, but with very poor results in deep-seated tumors, or in those with deep extensions. Of 40 such cases treated, 2 were apparently cured, and remained well for periods of nine and seven years respectively, but then developed recurrences and died. In about 20 of the remaining cases, in which treatment was faithfully kept up, great improvement was seen, in some instances the original tumor entirely disappearing, and recurrences being likewise destroyed, or kept in check for a time. That the lives of these patients have been prolonged and made more comfortable, there can be no doubt, but in no case was a true *cure* obtained. In several cases, subjected to apparently incomplete operation and then to radium treatment, good results were seen, but it is difficult to say in these how much was due to surgery and how much to radium.

Exner believes that the beneficial effect of radium in such cases is due in part to the shutting off of lymphatic channels by the connective-tissue proliferation which it excites, thus preventing metastases, as well as to the destructive action upon the cancer cells themselves.

As might be expected, Wertheim<sup>3</sup> warns against too enthusiastic expectations from radium treatment. In his opinion, the only way to determine that a real cure has been effected is either to keep track of the patient over a long number of years, or else to remove the uterus after treatment and examine microscopically practically the entire organ

<sup>1</sup> Wiener. klin. Wochenschr., 1913, vol. xxvi, p. 1650.

<sup>2</sup> Ibid., p. 1203.

<sup>3</sup> Ibid., p. 1648.

for traces of undestroyed carcinoma, for bits of tissue, excised for examination during treatment, do not permit of a final judgment; they may well show complete destruction in the areas from which they come, whereas the malignant process may be advancing unchanged in the deeper tissues.

Wertheim's personal experience covers 19 cases of uterine carcinoma treated with radium, and 3 treated with mesothorium. Of the 19 radium cases, 9 appeared clinically operable, 1 was a border-line case, and 9 were certainly inoperable. In 7 of the operable cases a radical operation was performed after the application of from 1700 to 20,000 mg. hours, applied for the most part in large doses over a comparatively short space of time.

In all the specimens, both from the patients treated with radium and with mesothorium, some effect was noted macroscopically and microscopically, but a complete disappearance of the tumor was seen only in a few where the growth was very superficial, *i. e.*, in cases in which apparently the same effect might have been produced by relatively minor procedures, such as excochleation and cauterization, or amputation of the cervix. A certain amount of action was seen also in the deeper tissues, but this was in no instance apparently sufficient to justify the belief that an ultimate destruction of all carcinoma cells in such regions might have been brought about.

Many unpleasant consequences, both of a general and local nature, were seen, such as malaise, loss of appetite, headache, diarrhea, necrosis, and sloughing, the latter being by no means always limited to the carcinomatous area. In cases which were operated upon after treatment, the operation appeared in many instances to have been made more difficult, on account of the great hyperemia and induration of the tissues which were produced, Wertheim's experience in this particular being quite at variance with that of Bumm and several other surgeons.

The author says that he intends to continue his experiments with radium, but in a very cautious manner, since he is as yet far from convinced that it has anything to offer in the treatment of uterine carcinoma which will displace the radical operation, where the latter can be applied.

A FRENCH REPORT ON RADIUM. In a report presented at the International Medical Congress in London last summer, Chéron and Duval<sup>1</sup> give their results in over 150 cases of uterine and vaginal carcinoma treated with radium during the past five years. They believe that the authors who have reported unfavorable results, and have therefore condemned radium treatment as worthless, have employed a faulty technique, and that their failure under these circumstances should not throw the entire method into disrepute. The most important point in the author's estimation is the use of *massive doses, well filtered*. In a

<sup>1</sup> Fortschr. a. d. Geb. d. Röntgenstr., 1913, vol. xxi, p. 229.

few cases, results may apparently be obtained with as small quantities as 10 mg. to 20 mg., but in the majority of instances such amounts are worse than useless, and failures resulting from treatment with these minimal doses of radium salts must be ascribed to the insufficiency of material, and not to the method *per se*. On the other hand, it appears that in a few instances, no result may be obtained even with sufficiently large dosage; here the fault is generally that the patient is in such poor condition that no reaction can take place as a result of the stimulus furnished by the radio-activity. The authors have encountered only 2 such cases in their series.

They believe that radium has not only a destructive, but also a *selective* action on carcinoma cells, exerting its effect more upon the malignant elements than upon healthy tissue. As an example of the rapidity with which such action can take place, they cite the case of a woman, aged forty-nine years, with an inoperable carcinoma of the cervix, involving the base of the right broad ligament and bladder, who was given two radium treatments, at an interval of two months apart. Clinically, the tumor entirely disappeared; fifteen months later she died (cause not given), and at autopsy no trace of cancer could be found in the body, grossly or microscopically. In another instance, two radium treatments rendered operable a previously inoperable carcinoma of the cervix, with involvement of the vagina and broad ligament. Microscopic examination of the extirpated uterus showed no carcinoma, but a lymph node from the pelvis contained a group of non-degenerated epithelial cells.

Out of a total of 158 cases treated, consisting chiefly of uterine and vaginal carcinomas, and of recurrences after hysterectomy, there was 1 definite anatomic cure (the case mentioned above), in 155 cases definite retrogression occurred (of these, in 93 this process was very marked, 46 of them probably representing true cures), and 2 were failures. Of the 46 *apparent* cures, 22 have now been under observation for a period of from one to four years since termination of treatment, and show as yet no signs of recurrence. In all the 46 cases there has been, so far as can be judged clinically, complete disappearance of the malignant tissue. In 12 patients, the treatment was kept up only until an inoperable condition was reduced to one of operability, when hysterectomy was performed. In 4 cases, radium treatment was begun immediately after hysterectomy for the purpose of preventing a recurrence. In all of these latter, although grossly all tumor tissue had apparently been removed, the conditions were such as to render the danger of recurrence especially great. In 1 of these patients, a recurrence did develop notwithstanding the treatment; the other 3 have been under observation for varying periods up to two years, without recurrence as yet. Among the cases classed under retrogression of more than one year's standing are several patients who had large growths, in whom only a part of the

malignant tissue could be removed at operation, radium treatment then being begun; one of these women has now been clinically free from all symptoms for over four years.

Chéron and Duval call attention to the fact that in comparing the results of operative and radiotherapy, we must remember that as yet practically only the most advanced and unfavorable cases, which are beyond reach of the former, are turned over to the latter, and that were the earlier ones, now subjected to operation, also included in the field of radiotherapy, this would probably have even more striking results to record than is the case at present. Whether we shall in the future be justified in doing this must, however, be left to the future to determine, for in the authors' opinion, this treatment is as yet too much in the developmental and experimental stage to displace surgery where the latter is applicable.

**RESULTS OBTAINED AT THE LONDON RADIUM INSTITUTE.** In a comprehensive report from the London Radium Institute, Pinch<sup>1</sup> gives the results of all cases of malignant disease treated there from August 14, 1911, to December 31, 1912. He says that in uterine cancer, radiotherapy will often bring about results which cannot be attained by any other known method of treatment. Hemorrhage is arrested, discharge is diminished and rendered inoffensive in character, ulcerations are healed, and pain is greatly relieved. Moreover, the rate of growth of the tumor is checked, sometimes completely arrested, and the surrounding infiltration and induration are so much lessened that in a few instances cases previously declared hopeless become easily operable.

The technique which has given the best results in the treatment of uterine carcinomas at the Institute is as follows: A tube containing 50 to 100 mg. of radium, screened with 2 mm. of lead and 3 mm. of rubber, is introduced into the cervical canal or into the posterior vaginal fornix, in addition a large flat applicator, screened with 2 mm. of lead, being placed on the abdominal wall over the fundus of the uterus. In the course of five to ten days a total exposure of from thirty to sixty hours is given, this being repeated at intervals of not less than six weeks. The action of radium is only local, and though it may, and often does, check the rate of tumor growth, yet in most cases dissemination will occur sooner or later, the disease spreading to parts beyond the effective range of the rays. During the time covered by the report, 41 cases of squamous carcinoma of the cervix uteri were treated; of these 3 were apparently cured, 19 were improved, 5 have died, and 2 were not improved; the remainder have stopped treatment, or were treated too recently to permit of any definite judgment as to the effects produced.

In the treatment of *vaginal growths*, some distinctly encouraging results have been obtained. Small, primary growths of the mucosa,

<sup>1</sup> British Medical Journal, 1913, No. 2717, p. 149.

unaccompanied by much deep infiltration of the vaginal tissues, may apparently be completely eradicated by an unscreened exposure of from one to three hours. With larger and more deeply infiltrating growths the radium is best applied heavily screened, with prolonged exposures of from thirty to sixty hours, extending over a week to ten days. This frequently checks the rate of growth, heals ulceration, and lessens the amount of infiltration. Eight cases are reported; of these, 3 received only prophylactic irradiation, 3 were improved, 1 showed no improvement, and 1 has abandoned treatment.

**CELL CHANGES PRODUCED IN DEEP TISSUES BY THE X-RAY.** A series of studies of the histological changes produced in the deeper tissues by *x-ray treatment* are reported from the Freiburg Clinic by Aschoff, Krönig, and Gauss,<sup>1</sup> the results being in general similar to those of Haendly, discussed above. The patients from whom the specimens were obtained were all subjected for varying periods of time to enormous doses of Röntgen rays, given highly filtered, according to the well-known Freiburg technique, the object being to determine just how much destruction of malignant cells could be accomplished in deep tissues, which could be reached by the rays only after these had passed through the more superficial layers.

The first case was that of a woman (age not given) with an inoperable carcinoma of the stomach. Two bits of tissue excised from an ulcerated area at an exploratory laparotomy showed extensive adenocarcinoma. After three and a half months of *x-ray treatment* an attempt was made to perform a gastro-enterostomy, a bit of tissue being excised at the same time for examination. This showed intense inflammatory changes, granulation tissue, and some vacuolated cells resembling endothelium, but nothing which could be recognized as carcinoma. A mesenteric, lymph node, removed at the same time, showed, however, the typical picture of a metastatic adenocarcinoma. Two days later the patient died. Sections taken at autopsy from the wall of the ulcer showed in places likewise only fibrous tissue and active inflammation, in other areas, however, were a few scattered bits of carcinoma tissue, and groups of epithelial cells undergoing mucoid degeneration. Numerous metastases were present in lymph nodes and in the liver.

The second case was a woman, aged fifty-seven years, with a squamous carcinoma of the cervix. The cancer cells were "unripe," *i. e.*, showed no tendency to cornification. During eight months of treatment no less than 17 excisions were made from the cervical tissue; at the end of this time the patient died, and came to autopsy. The malignant process had gone on to perforation of the rectum, and was threatening to perforate the bladder at the time of death. Examination of the specimens removed during life and at autopsy showed some formation of scar tissue,

<sup>1</sup> Münch. med. Wochenschr., 1913, vol. ix, p. 337.

and a marked change in the character of the carcinoma cells, which had become "riper," showing much cornification and pearly body formation; in most areas they also showed extensive degeneration, but were by no

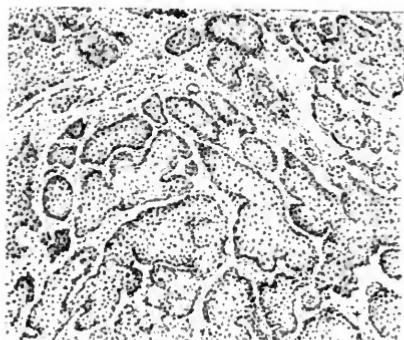


FIG. 95

means actually destroyed. Fig. 95 shows the histological appearance of the tissue before treatment was begun, and Fig. 96 that presented by a bit excised five months later.

Case III was a woman, aged fifty-five years, with inoperable carcinoma of both breasts. Tissue excised for examination, both from one breast



FIG. 96

and an axillary lymph node, showed the typical picture of a tubular carcinoma. The patient lived for six months, during which time she was subjected to *x*-ray treatments, and 12 excisions of tissue were made,

9 from one breast, and 3 from the other. Similar changes in the character of the carcinoma cells as occurred in the preceding case were observed here, together with much connective-tissue hypertrophy, but there was nothing approaching complete destruction of the malignant tissue, even in the breast, while the axillary nodes were full of practically unaltered carcinoma cells.

In addition to these 3 cases which came to autopsy, 5 patients are still under observation and treatment, excisions of tissue being made from time to time. Two of these are suffering from cervical and 2 from breast carcinomas, all inoperable. In these, the results so far obtained are similar to those recorded above. The fifth patient is a woman, aged fifty-three years, with a recurrence in the abdominal wound a year after



FIG. 97

a radical operation for carcinoma of the cervix. A bit of tissue excised from this mass in the abdominal wall showed the typical picture of a cervix carcinoma (Fig. 97). A month later, the appearance had changed to that represented in Fig. 98; the cells have become larger, more irregular, and have taken on more the appearance of the slow-growing tumors of the "cancroid" type; there are still many undegenerated nuclei, however, some showing mitosis, so that proliferation has evidently not been entirely checked. Two bits of tissue removed after seven weeks of treatment showed almost nothing but fibrous tissue, in which only one small cancer nest could be found (Fig. 99), and by another month absolutely nothing suggestive of malignancy could be discovered in the excised bit of tissue. This result was only illusory, however, for subsequent excisions showed again carcinomatous areas, whose character

changed from time to time, some samples of tissue showing an apparent retrogression, others again an improvement, as compared with previous examinations. In all, 9 excisions were made during the course of a year, and the patient is still under treatment.

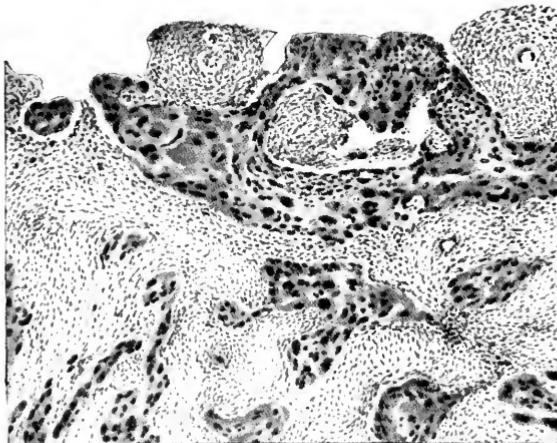


FIG. 98

In summing up their results, the authors conclude that there is certainly an influence produced on the carcinoma cells *within the immediate area of radiation*. This consists in a reduction in the quantitative pro-

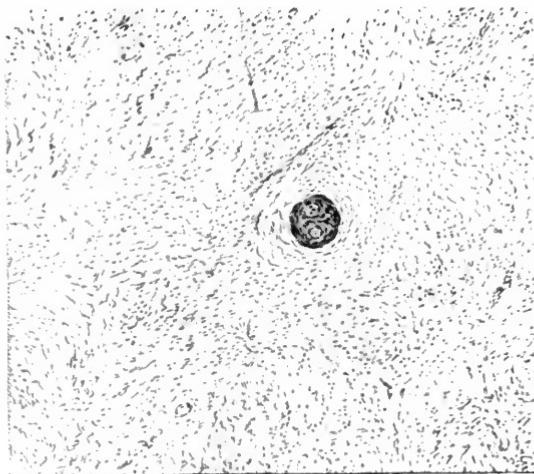


FIG. 99

portion of carcinoma tissue present, with a corresponding increase in the dense fibrous tissue; an inflammatory reaction is set up, and there is an alteration in the character of the carcinoma cells, which become

"riper" (evidenced by cornification, and the formation of pearly bodies), and apparently less malignant. There is also a reduction in the energy of cell division, resulting in giant-cell formation, swelling and vacuolation of the protoplasm, etc. These effects are produced, however, only in the direct field of radiation—metastases in structures outside of the exposed area show no reduction in malignancy, nor diminution in growth.

So far as these authors have been able to determine, no deleterious influence was exerted on normal structures lying in the exposed fields, notwithstanding the application of enormous doses, with the single exception of a small area of necrosis, which was produced in the intercostal muscles and superficial portion of one lung in a case where the dose given was much larger than necessary. In one other case small areas of necrosis were found in the liver, but it was not certain that these were due to the  $\alpha$ -rays.

In none of the cases was there complete destruction of the carcinomatous tissue. The great difficulty appears to lie in the fact that as the character of the carcinoma cell is gradually altered by the irradiation, it approaches biologically more and more to the normal body cells, so that there is danger of injuring these if sufficiently powerful rays are used still to act on the carcinoma cells. The authors express themselves, however, as being far from discouraged by these results. They have at least demonstrated that by the use of the  $\alpha$ -rays alone there can be produced in deeply seated carcinoma tissues histological changes similar to those which have long been known to occur in superficial growths, namely, a reduction in the degree of malignancy, a slowing of growth, and to a certain degree at least, a destruction of cells. The total failure to produce any appreciable changes in metastatic foci, lying outside the immediate field of exposure, shows, however, that to be really effective  $\alpha$ -ray treatment should be applied before extensive metastasis has occurred, and the authors suggest that in treating any given form of tumor it would be well to irradiate the corresponding areas of regional lymph nodes, as well as the primary growth.

EXPERIMENTAL INVESTIGATIONS OF THE TISSUE CHANGES CAUSED BY RÖNTGEN RAYS. Some interesting results of animal experimentation, which, however, appear to have considerable bearing upon clinical work, have been reported by Lacassagne.<sup>1</sup> He has been particularly interested in studying the effects produced upon the ovaries by exposure to considerable doses of  $\alpha$ -rays, and also in determining whether or not any deleterious changes may be caused in important organs which there is no intention of affecting, but which cannot be entirely excluded from the path of the rays. Some of Lacassagne's work in the latter direction has been previously referred to in this department.<sup>2</sup>

In order to study the ovarian changes he subjected a number of rabbits

<sup>1</sup> Ann. de Gyn. et d'Obst., 1913, vol. xl, 2 s., p. 449.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1913, p. 233.

to a single dose of 40-X to 44-X through an aluminum filter, 4 mm. thick, and then killed them at increasing periods subsequent to exposure. He has found, in accordance with other investigators, that in the first place, immediately after the irradiation, almost all of the follicles appear to be undergoing degeneration, this being the more pronounced in the riper ones, by the fifteenth day all developing follicles having disappeared. Here and there, however, a few intact primordial follicles are always to be found. Secondly, the interstitial gland, so well developed in rodents, degenerates almost completely. By the third or fourth month the ovary appears entirely sterile; it has shrunken to an insignificant strand of tissue, weighing not more than one-fiftieth as much as a normal organ, and shows microscopically merely a bit of fibrous connective tissue surrounding a central packet of bloodvessels.

From such findings most authors have concluded that the ovarian atrophy is complete and permanent. Lacassagne has found, however, that if the animal is allowed to live longer, a certain amount of reparation takes place; first the interstitial gland is reconstructed by a transformation of some of the connective-tissue cells into secreting elements, then the scattered primordial follicles, which have escaped destruction, start to develop, so that fecundity may be reestablished, at least temporarily. No new follicles are formed, however, and a second, weak dosage of  $\alpha$ -rays, given about six months after the original, so as to reach the newly developing follicles, will assure a definite destruction of all reproductive power.

In applying this form of treatment to larger animals, however, three difficulties are met with: The ovary is at a greater distance from the focal point of the tube, there is a greater amount of interposed tissue, and the exact location of the ovaries is uncertain. That these factors are of considerable moment in attempting to produce sterilization with a single massive exposure is shown by the fact that Lacassagne has seen a single dosage of 40-X, given to a good-sized dog through a 4 mm. aluminum filter, produce gradual cachexia and finally death after several months, due to intestinal injury (atrophy of the glands of Lieberkühn, ulcerations, and perforations), and yet the ovaries still contained many healthy follicles. From these experiments, Lacassagne concludes that the action seen clinically of  $\alpha$ -rays on myomas is a *direct* one on the tumor itself, and not, as has been almost universally assumed, purely secondary to the ovarian changes. He believes, therefore, that in treating growths of this type the rays should be applied directly over the tumor tissue, and not to the ovarian regions. It is undoubtedly possible, however, by a series of weak doses to destroy the larger follicles, and thus to influence menstruation, but great care should, in his opinion, be taken not to injure the surrounding organs, especially the intestines.

**Chemotherapy. USE OF COMBINED CHEMO- AND RADIOTHERAPY.** Since the first real interest in chemotherapy as applied to malignant

disease was stimulated by Wassermann's famous experiments in the treatment of mouse cancers by the intravenous injection of an eosin-selenium combination,<sup>1</sup> comparatively little progress in this field appears to have been made, at least from the clinical stand-point, although this year we are able to present a few more reports of such attempts than was the case a year ago. Chemotherapy alone seems, so far at least, to have fallen far short of a realization of the hopes that were aroused by the earlier experimental results; but some extremely interesting work has been done by combining it with radiotherapy, in the hope that by this double attack a more complete and rapid destruction of malignant tissue may be brought about than by either of the methods alone. In this connection, a case reported by Seeligmann<sup>2</sup> is of great interest. The twenty-four-year-old patient had an intraligamentous, solid ovarian tumor, weighing ten pounds, which was removed, histological examination showing it to be a spindle-cell sarcoma. Nine months later, the girl again presented herself, with a recurrence on the same side as the primary tumor. In six months more the entire abdomen had become filled with hard masses, and there were evidences of involvement of the spinal column. At a second laparotomy the recurrent growth was found to be retroperitoneal in situation, and larger than the original. There was no possibility of operative removal.

A few days later intravenous injections of 0.1 gram "arsazetin" were begun, combined with *x*-ray treatments, two series of these, each lasting about twelve days, being given, the total dosage amounting to 121-X. In each series the tube was applied to ten different surface areas, the rays being filtered through 1 to 2 mm. of aluminum. At first, the arsazetin injections were given once a week for four doses, and were then intermittent for four weeks, when a fifth dose was given. Chills and fever occurred after the second injection, but were only of brief duration. The improvement was remarkable; the tumor steadily decreased in size, the pains in the spinal column disappeared, the patient increased markedly in weight and color, and was soon able to get up. An *x*-ray examination at this time showed the twelfth dorsal and first lumbar vertebrae to be involved, but the lesion was apparently in progress of healing. After eight weeks of treatment, no remains of the tumor were to be felt, and the patient had regained the ability to walk upright, which she could not do previously on account of severe pain in the spinal column. She was discharged after eight weeks of treatment, but was subsequently given two further injections of 0.1 gram of arsazetin at intervals of four weeks, and a Röntgen exposure of 50-X. She has remained for six months entirely well, showing no sign of tumor formation, or of metastasis in the spinal column.

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1912, p. 170.

<sup>2</sup> Münch. med. Wochenschr., 1913, vol. ix, p. 637; Deut. med. Wochenschr., 1913, vol. xxxix, p. 1310.

Seeligmann is now trying this combined chemotherapy and radiotherapy on a series of carcinoma cases, apparently with encouraging results, which, however, are to be reported later. He is only using it as yet in recurrent cases, or after operation to prevent recurrence. He thinks the invading cancer cell has a certain affinity for the arsenic, which as a result of the radio-activity, is thrown out of its chemical combination, and exerts in the nascent state a destructive action on the cancer cells, and that under these conditions, therefore, the quantity of  $x$ -rays required does not have to be so large as when the destructive effect is dependent upon them alone. Moreover, the problem in treating inoperable carcinoma is not only to destroy the older, less resisting cells, which can be done with radiotherapy, but also the younger cells, the newer outgrowths at the edge of the tumor, and in distant locations, which are not affected by it. These, Seeligmann hopes, may be reached by the chemical substances circulating in the blood. He also suggests that if the parasitic theory of cancer is correct, good results from this treatment may be due to a destructive action of the arsenic upon the parasite.

Klotz<sup>1</sup> also emphasizes the fact that in order to accomplish anything in the treatment of carcinoma with radiotherapy alone, enormous doses of both  $x$ -ray and radium preparations are necessary, so that even in institutions having free access to large quantities of radium, the cost of such treatment is enormous, and it is therefore necessarily limited to a comparatively few patients. He has therefore been attempting to attack the cancer cell not only from the outside, but also from within—from the vascular system. For this purpose he has tried intravenous injections of "tumoraffin" substances, and has found that by this means the necessary radiodosage can be greatly reduced, and yet excellent results be obtained. The results are due, he believes, to an action exerted on the nuclear chromatin of the carcinoma cells themselves by the chemical substances, and to an artificial hyperemia which is produced in the tumor, rendering it more easily destroyed. Another possibility is that within the tumor itself, when subsequently exposed to the action of  $x$ -rays or radium, secondary rays are produced from the tiny particles of the colloidal metal deposited in the tumor substance.

The technique which Klotz now adopts in a typical case of inoperable carcinoma of the cervix is as follows: First an intravenous injection of 5 c.c. of "electrocobalt" is given; immediately following this, the tumor is subjected to a Röntgen treatment of 400-X to 450-X in the course of two days, applied from a large number of portals of entry, as follows: ten abdominal fields, ten fields on the back, two vulvar areas (immediately below each tuber ischii), and eighteen vaginal exposures. After a lapse of nine days, a second intravenous injection of 5 c.c. of electrocobalt

<sup>1</sup> Deut. med. Wochenschr., 1913, vol. xxix, p. 2554.

is given, followed by a vaginal treatment with radium (about 800 to 1000 mg. hours).

After another interval of nine days, the patient receives a third intravenous injection of electrocobalt (5 to 10 c.c., the dosage being controlled by the examination of the urine for albumin and casts), then a Röntgen treatment of 400-X to 450-X, and so on, alternating between *x*-rays and radium at nine-day intervals, the intravenous injection of the colloidal metal being given each time immediately before exposure to either form of radiant energy.

Klotz reports in this paper one case, a recurrent carcinoma. The patient was given a total dosage of 1148-X and 9680 mg. hours. The treatment lasted three and one-half months, by which time the tumor had completely disappeared; the report was written only two months after the cessation of treatment, but up to that time no signs of recurrence had become manifest.

In another article, Klotz<sup>1</sup> says that he has tried this combination of chemotherapy and radiotherapy in 13 cases of uterine carcinoma. Although this report likewise is merely preliminary and he cannot speak of final cures, he says that he has produced distinct retrogression of the carcinoma—not only has hardening, shrinkage, and desiccation of the superficial neoplastic tissue occurred, but also of the deeper lying metastases in the pelvic connective tissue. He believes that while chemotherapy may be of little value alone, used thus as an adjunct to radiotherapy, it will prove to be of great service in permitting a considerable reduction in the amount of the latter necessary to produce a given result.

LOEB'S COLLOIDAL COPPER SOLUTION. Some clinical experiments with the intravenous injection of a colloidal copper preparation, similar to those previously reported by Loeb,<sup>2</sup> have been undertaken by Weil<sup>3</sup> on 12 patients suffering from various types of inoperable carcinoma. He found that in a number of instances a phlebitis gradually developed following the injections; in some cases this amounted to nothing more than a slight induration of the veins with some pain, in others, however, there was extreme induration, with thrombosis, severe pain, edema, and all the concomitants of a severe phlebitis and thrombophlebitis, which was, however, in all probability, merely the result of a chemical irritation of the endothelium, since in no case was there any evidence of embolism or infarction, and no constitutional symptoms developed which might have been attributable to the phlebitis, other than a low grade of pyrexia, or of general malaise. In some patients all the available veins eventually became obliterated, so that none were left accessible for injection.

The constitutional symptoms varied—chills and a rise of temperature

<sup>1</sup> Münch. med. Wochenschr., 1913, vol. ix, p. 1704.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1913, p. 190.

<sup>3</sup> Journal of the American Medical Association, 1913, vol. lxi, p. 1034.

were marked in some patients, but were absent in others, and nausea and vomiting were at times quite troublesome. In none of the patients, however, was there any such improvement in general condition as is reported by Loeb; they practically all showed a loss of 5 to 10 pounds in weight, and a reduction in the hemoglobin of from 10 to 20 per cent. during treatment; but on the other hand, in some cases, improvement took place upon stopping the treatment. Occasionally a moderate degree of hemoglobinuria gradually developed following the injections, probably due to some toxic influence of the copper on the red-blood corpuscles. There was also a slow toxic action on the kidneys, evidenced by a small amount of albumin in the urine.

Examination of two tumors, one removed at operation and the other at autopsy, after prolonged treatment, showed no trace of copper in the tumor tissue, nor was any found in the kidneys of the autopsy case, but it was demonstrable in the liver. Weil thinks it very doubtful, therefore, that copper has any such specific affinity for tumor tissue as has been claimed. Circulatory changes, swelling, peripheral hyperemia, and altered character of the discharge were noted, but these, he points out, have no relation to the actual cure of the tumor, and are phenomena which cannot be considered essential, a *demonstrable reduction in the size of the growth* being the only symptom upon which any definite reliance should be placed.

Of the 12 patients treated by Weil for various malignant conditions, the injections were stopped in 4, when less than twenty had been given, owing to undesirable symptoms developing; the other 8 received a fairly thorough course of treatment (up to 30 injections). Every phenomenon described by Loeb and other authors, such as a subjective improvement in spirits, in apparent strength, in appetite, and in the character of the discharge, increased hyperemia of the tumor, etc., were seen except the crucial one of actual diminution in size; this did not occur in a single instance, so that Weil concludes that, with the present technique at least, the administration of colloidal copper must be relegated to the ranks of the countless other remedies that have been enthusiastically hailed as the possible real cure for cancer, tried and found wanting.

**CLINICAL WORK WITH SELENIUM.** Touche<sup>1</sup> has followed Wassermann's work somewhat more closely, in that he has been treating a series of carcinoma patients with *colloidal selenium*, administering this, however, not intravenously, but by intramuscular injection into the gluteal region. His method is to give one injection of 5 c.c. weekly for three doses, and then to stop for a while, further treatments being governed by the course of the case. These injections cause, as a rule, no more discomfort than do deep mercuric injections in syphilis. Touche

<sup>1</sup> Bull. mém. Soc. méd. des Hôp. de Paris, 1913, vol. xxix, p. 451.

reports having treated in all 27 patients, among these 2 had a carcinoma of the breast, and 4 of the uterus. In all of these the treatment greatly ameliorated the subjective condition of the patient, without, however, in any way leading to an actual cure. In the cases of breast carcinoma, it appeared to reduce the adenopathy, to mobilize the breast on the underlying tissue, and to retard somewhat the progress of the disease. In the uterine cases, it had a very marked action in destroying fungosities, causing them to be replaced by hard, nodular, non-sloughing masses. It suppresses discharge and hemorrhage, as well as pain, and gives to the patients a subjective illusion of cure. It seems to retard, somewhat, the extension of the cancerous growth, but has no permanent curative action. Its most favorable action was seen in carcinomas of the uterus and of the rectum, in which conditions the author considers that it is certainly one of the most valuable *palliative* forms of treatment at our command today.

Another series of investigations based on Wassermann's work is reported by Braunstein.<sup>1</sup> Since the original eosin-selenium compound, used by the former, has not proved applicable to human therapeutics, owing to its poisonous qualities, Braunstein has made a combination of selenium, which is the essential tumor-destroying substance, with methylene blue as a "carrier," this latter material being just as diffusible as eosin, but practically harmless in any quantity. To this combination, iodine was added for two reasons; because carcinoma cells are known to exhibit a marked affinity for iodin, and because iodin increases autolytic processes in the animal body.

With this combination of selenium, methylene blue, and iodin, Braunstein has treated 18 cases of malignant disease, among these 2 carcinomas of the breast, 2 of the vagina, and 1 of the uterus. For comparison, a combination of methylene blue and iodin alone, without selenium, was given to 2 other patients, no changes whatever being noticed in these during a two-weeks course of treatment. In practically all the others, however, marked objective and subjective improvement occurred, consisting in a diminution or disappearance of pain, a picking up of the general condition, and in many instances, an increase in weight. Where ascites was present, this decreased or disappeared; a shrinkage of the tumor mass, increased mobility, and reduction in the size of involved lymph nodes were also noted.

The injections, which were given intravenously, were for the most part well borne, though they were often accompanied at first by a temperature rise, with chills. All the cases treated were in an advanced and hopeless condition, and though unable to record any cures, the author considers the benefits produced sufficient to warrant further trials with the method, which at least is entirely harmless.

<sup>1</sup> Berl. klin. Wochenschr., 1913, vol. 1, p. 1102.

**EXPERIMENTS WITH COLLOIDAL GOLD.** Lewin<sup>1</sup> reports some experiments following, in a general way, the work of Neuberg and Caspari<sup>2</sup> with intravenous injections of colloidal forms of the heavy metals. Lewin has used salts of gold, on account of the known action of these in destroying bloodvessels, his hope being in this way to destroy the neoplastic tissue by causing intratumoral hemorrhage. The experiments were all done with mouse cancers, using gold-and-sodium-chloride, cyanide of gold-and-potassium, and a colloidal preparation sold under the name of "goldsol." All of these are capable of undergoing, in the tumor substance, a transformation into colloidal gold. The effects produced by intravenous injections of these preparations were very marked. After two injections all the changes described by Neuberg and Caspari were seen in the tumors—extensive hemorrhage into the tissue, with blood extravasation, and the formation of blood-stained degenerative products within the tumor substance. After three or four injections, the tumor had generally become transformed into a friable, necrotic, and hemorrhagic mass. The action of these gold preparations seems to be purely upon the walls of the capillary bloodvessels, however; they do not appear to have any direct autolytic effect upon the tumor cells themselves. The action appears, moreover, limited to the vessels of the tumor, perhaps due to the fact that these are the youngest in the body, and are therefore the least resistant, or that the chemical as it circulates in the blood is in large part mechanically filtered out by the tumor, and therefore acts here in a more concentrated form than elsewhere.

**Other Aspects of the Cancer Problem.** POPULAR EDUCATION CONCERNING UTERINE CANCER. Aside from the investigations along the lines discussed above, radiotherapy and chemotherapy, there is nothing new of prime importance to be reported in connection with uterine cancer during the past year. Summaries of results obtained from the *radical operation* continue to appear from time to time, especially in the German literature, but these have added but little to what is already known upon the subject, a fairly extended discussion of which has appeared in these pages for several years past. With the excitement attending the radium furore, however, the interest of many of the most important continental surgeons appears to have been in large part diverted from the radical operation, which, so far as the literature is concerned at any rate, has distinctly fallen into second place. This is also undoubtedly due in part to the fact, which has been becoming more and more evident of late, that the radical—or so-called "Wertheim operation"—has reached, in many hands, a fairly definite stage of development, beyond which but little or no advancement can be expected. The results obtained with it in most of the important German clinics

<sup>1</sup> Berlin. klin. Wochenschr., 1913, vol. 1, p. 541.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1913, p. 188.

are fairly uniform; its limitations are pretty definitely recognized, and the main points of technique have been thoroughly worked out, so that the operation, although extensively practised, has ceased to be the burning question that it was a few years ago.

Quite another phase of the subject, namely, the attack upon the cancer problem from the educational side is, however, assuming more important proportions each year. In this country, a new society for this purpose has been recently organized—the "American Society for the Control of Cancer."<sup>1</sup> Its membership is open to both laymen and physicians, and its purpose is to do everything possible toward educating the public in a rational manner concerning cancer. It aims to be national in scope, and has already secured the hearty endorsement of the American Medical Association. The purpose of the society is to collect extensive statistical data, on the basis of which authoritative articles will be prepared, showing that the menace of cancer can be controlled by early diagnosis and treatment.

Some definite and very practical suggestions as to the methods of carrying on such a campaign are given in a paper read before the American Gynecological Association by Taylor.<sup>2</sup> He emphasizes the importance of educating the laity as well as the physicians, and sees no reason why the public should not be brought to the same point with regard to uterine cancer as with regard to appendicitis; as he truly says: "It is no longer necessary to urge an operation for appendicitis; as soon as the diagnosis of acute appendicitis is made, the family wants to know how soon it can be done, and to what hospital the patient should be sent. The physician who makes a mistake in the diagnosis of appendicitis, or neglects an early operation, risks his reputation in the community in which he lives. This is as it should be, and as it should be relative to carcinoma of the uterus, and as it will be when the laity has the same knowledge of carcinoma of the uterus that it now has of appendicitis. The mere fact that the physician knows that his patient has been taught this simple, clean-cut fact will make him more alert to the condition himself."

In conducting such a campaign, Taylor thinks that legitimate use can be made of the publicity and press-agent methods in constant use in the business and political worlds. In view of the readiness with which the public press nowadays accept articles on eugenics, venereal diseases, and other subjects which would have been tabooed a few years ago, there should be no difficulty in getting a wide circulation for articles on carcinoma of the breast and uterus. The routine work must be chiefly carried on by a paid lay staff, under constant medical supervision, the educational work that has been done on tuberculosis furnishing an excellent model of how to accomplish the most results with the least

<sup>1</sup> Journal of the American Medical Association, 1913, vol. lxi, p. 617.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, 1913, vol. xvii, p. 720.

expenditure of energy. In this work, the central controlling force has been located in New York, with a large number of subcommittees throughout the country. Short, pithy articles, of from one hundred to five hundred words, on the relationship of tuberculosis to some popular subject, have been prepared and mailed as news items to about 800 newspapers every two weeks or so, a large amount of publicity being thus secured at comparatively small expense. The local committees have charge of lectures, exhibits, the distribution of literature, etc., all under the direction of the central body.

In addition to the adaptation of such methods to the cancer problem, Taylor urges that arrangements should be made by which government laboratories would be available to every practitioner for the histological examination of suspicious tissue discharged or curetted from the uterus, in a manner similar to that in which facilities for the bacteriological diagnosis of diphtheria are now placed at his disposal. The author also makes a plea for the gathering of reasonably accurate and complete statistics upon the uterine cancer, the woful lack of which in this country was brought out so forcibly in the symposium on the subject presented before the American Gynecologic Society two years ago.

In addition to the methods outlined above, a constant hammering at the medical profession by means of short articles appearing in repeated editions of medical journals, by sending out cards containing a summary of the symptoms of uterine cancer with medical society notices, etc., is advocated; the importance of impressing every graduating class of trained nurses with their responsibility in the matter, and of attempting to reach the midwives, is also emphasized.

That tangible results are obtainable from such a campaign of education is shown by a report from a corner of the world which we do not ordinarily associate with a high degree of enlightenment or progress as far as medical science is concerned. Knorre<sup>1</sup> gives the results of a campaign of education which has been carried out in the Baltic States of Russia by the Gynecological Section of the "Society for the Prevention of Carcinoma," founded in 1908, along the lines laid down by Winter.<sup>2</sup> The methods which he originally suggested were followed closely, letters being sent to general practitioners and to midwives, and articles prepared for the lay press. Three years after the institution of this campaign, letters were again sent out to a large number of physicians and hospitals with the following questions: (1) Have women, suffering with carcinoma of the uterus, applied for examination during the last trienium more promptly after the appearance of the first symptoms than formerly? (2) Have you seen cases that have been allowed to go on developing from ignorance or carelessness of physicians or midwives? (3) Has the campaign of publicity done good or harm?

<sup>1</sup> Petersb. med. Ztschr., 1913, vol. xxxviii, p. 30.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1912, p. 171.

In answer to the first question, reports covering 504 cases were available, and the results must be considered decidedly encouraging, 39 per cent. of the patients having consulted a physician within three months of noticing the first suspicious symptom, as against only 15 per cent. found at a former investigation. With regard to the second question, 27 cases (5 per cent.) were reported in which local treatment had been persisted in, or in which douches, etc., had been prescribed, without any investigation on the part of the physician first consulted. With regard to the last question, all answers have been to the effect that the publicity campaign has done good, but that the effect is only temporary, as any one series of articles is seen by comparatively few people, and is quickly forgotten by many of those that do see it. Only a few physicians report having seen the development of any undue omophobia, and those who have had patients consult them merely from fear of cancer believe that the good accomplished far outweighs any such harm.

**VALUE OF CYSTOSCOPY IN DIAGNOSIS OF UTERINE CANCER.** Violet and Murard<sup>1</sup> are certain that in some cases cystoscopy is of the greatest value in determining the operability or inoperability of uterine carcinoma, notwithstanding the criticism which has been applied to this means of diagnosis by some surgeons. Irregularities in the trigone, or on the bladder wall above it, projections of mucosa into the cavity similar to that seen in prostatic hypertrophy, often accompanied by little ridges and depressions, which present in the cystoscope an appearance of miniature snow mountains, are the first changes generally seen in carcinomatous invasion. Bullous edema and edematous plicæ are sometimes seen in the trigone, and indicate some involvement of the submucosa. A peculiar appearance, sometimes noted not in the trigone, but in the fundus, is a pale, dull mucosa, crossed by fine, irregular, reddish lines, outlining irregular rectangular or lozenge-shaped areas, the whole presenting a general aspect of cracked porcelain. This condition the authors consider especially significant of advanced involvement of the bladder wall; it is often found in cases in which to palpation this appears entirely free, since it occurs particularly when the carcinoma extends upward through the cervical canal and attacks the bladder only in the upper portion. Ulcerations and vegetations indicate an involvement of the mucosa itself, but care must be taken not to mistake for these lesions due to an old cystitis, which are often present in conjunction with uterine carcinoma, without any direct involvement of the bladder wall.

The ureteral orifices may be difficult to find, or on the other hand, they may be prominent, gaping open, and situated at the apex of a little edematous papilla, this latter condition being always very suggestive

<sup>1</sup> Rev. de Gyn. et de Chir. Abdom., 1913, vol. xx, p. 129.

of stricture somewhere above. In a few instances, actual little projections of neoplastic tissue will be seen about the ureteral orifices. The manner of ejaculation of urine from the ureteral orifice, as demonstrated by chromocystoscopy, has not given the authors any reliable data, but ureteral catheterization may, in their opinion, give information of great value as to the involvement of the ureter, and the functional activity of each kidney.

POINTS IN THE TECHNIQUE OF THE RADICAL OPERATION. Bumm<sup>1</sup> believes that the most careful and thorough covering with peritoneum of all raw areas left after any operative procedure is of the greatest importance, and especially after a radical operation for carcinoma of the cervix. The gradual adoption of this principle, with a coincident reduction in the use of drainage, is responsible, he thinks, for the steady fall in mortality which has occurred in his practice. Bumm's worst results were obtained when he was in the habit of draining the pelvic cellular tissue with gauze packs carried out through the vagina, his mortality in 138 cases averaging almost 30 per cent. In almost one-third of these cases, suppuration and necrosis occurred in the tamponed cavities, with resulting necrosis of the peritoneum over them, and ascending peritonitis.

Better results were obtained when he abandoned gauze drainage of the pelvic tissue, and united the loosened bladder and rectum with the edges of the vagina, closing the raw areas of the broad ligament with running sutures. For a time he could not get away from the drain, however, but now placed it in the lower angle of the pelvic peritoneum, and carried it out through the vagina. During this epoch his mortality was 21 per cent., still chiefly due to ascending peritonitis.

All this has been changed since omitting all drains and tampons. His present technique is to close off carefully all pelvic raw surfaces from the general peritoneal cavity with a double layer of sutures, using no drainage of any kind. In the last 100 cases, operated on according to this technique, but similar in all other respects to the earlier series, the mortality was only 6 per cent. (6 deaths, only 4 of these, however, being due to peritonitis, the others to cardiac insufficiency).

Bumm believes that the tampon serves only to collect wound-secretion, which forms an excellent culture medium for the pathological organisms that are always present in carcinomatous tissue. When, however, the peritoneum is carefully closed at all points, leaving everywhere a smooth surface with no raw areas, it can easily handle considerable quantities of even virulent organisms. Great care should, however, be taken to prevent the spread of infection from the carcinomatous area during operation, an important point in this regard being not to operate on patients with carcinoma of the cervix in the presence of the slightest amount of fever.

<sup>1</sup> Zentralbl. f. Gyn., 1913, vol. xxxvii, p. 1.

Maxwell<sup>1</sup> says that he has found the regular Wertheim clamps for closing off the lower end of the vaginal cuff unsatisfactory, as no rigid-hinged forceps can effect equal pressure on all the enclosed tissue from heel to tip, nor is the difficulty completely overcome by the application of a forceps from each side, with tips well overlapping. Maxwell has,

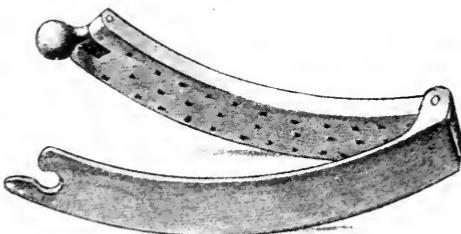


FIG. 100.—Vaginal clamp. In front is the thin, pliable blade, with a slot to receive the swivel on the rigid serrated blade.

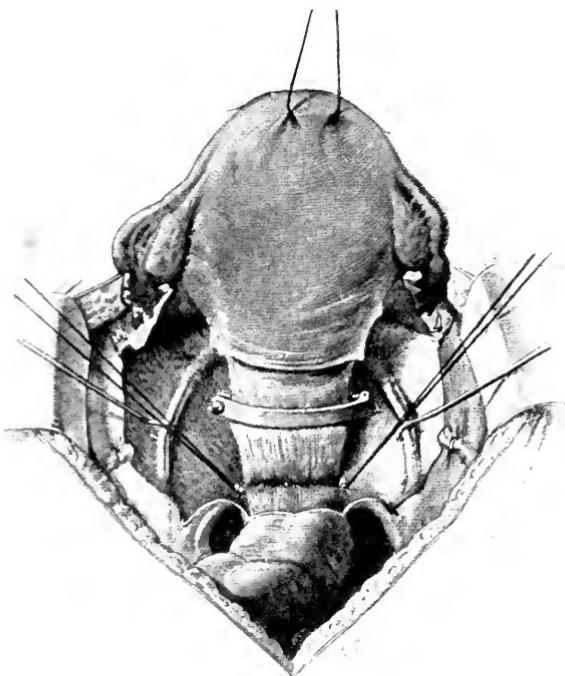


FIG. 101.—Clamp in place; view from behind.

therefore, devised the clamp shown in Figs. 100 and 101, its special features being that the anterior arm is slightly longer than the posterior, and is somewhat springy, so that it can bend around the enclosed tissue,

<sup>1</sup> Proc. Roy. Soc. Med., 1913, vol. vi, Obst. and Gyn. Sect., p. 262.

and thus cause equal pressure throughout its entire length. A slight convexity has been given to the lower edge to facilitate the division of the vagina below it. The author says that he has found it to be easily applied, and to perform its function well.

PALLIATIVE METHODS OF TREATMENT FOR INOPERABLE UTERINE CANCER. POWDERED SUGAR. Berczeller<sup>1</sup> suggests a rather novel method of palliative treatment for cases of inoperable carcinoma of the cervix, namely, the application of *powdered sugar*. This treatment is extremely simple, but has been, in his hands, very efficacious in action, causing rapid disappearance of the offensive odor and discharge, and a reduction in the amount of hemorrhage; the surface of the tumor mass becomes dryer, the mass itself shrinks, and there is generally some improvement in the patient's general condition.

*Technique.* The cervix is exposed in a cylindrical speculum, and wiped dry; the speculum is then half filled with powdered sugar, a strip of iodoform gauze inserted, and the speculum removed, this treatment being repeated from once a day to once a week, according to circumstances.

Bainbridge<sup>2</sup> is a strong advocate of not simply leaving all patients with inoperable pelvic cancer to their fate, believing that in many instances great relief can be afforded, at least temporarily, by the method described below. This is not indicated in all cases of pelvic carcinoma, but may be under the following circumstances: (1) When hemorrhage, which threatens death, cannot be controlled by other means. (2) When hemorrhage has been so severe or so frequent as to warrant the fear of a fatal return at any time. (3) When hemorrhage is sufficient to cause a drain upon the patient's vitality. (4) When the disease is so extensive as to render curettage dangerous because of hemorrhage. (5) When there is reason to believe that by controlling, to a certain degree, the progress of the disease, the pain, fetor, and discharge may be lessened. (6) When it is possible by this means to relieve various pressure symptoms (7) When associated conditions call for an exploratory laparotomy. (8) When all other means have failed to give relief, the patient demands that something more be done, and there appears to be some hope of relieving suffering or prolonging life.

The operation which Bainbridge advocates has for its chief object, first, a diminution of the blood-supply to the area of cancerous involvement, thus retarding the malignant process, and secondly, a blocking-off of the avenues of absorption of cancer cells and toxic products by removing, as far as possible, all lymphatic glands and vessels between the receptaculum chyli and the obturator foramen on each side.

*Technique.* The ovarian arteries are ligated just above the brim of the pelvis, and the ovaries, tubes, and upper portions of the broad

<sup>1</sup> Zentralbl. f. Gyn., 1913, vol. xxxvii, p. 852.

<sup>2</sup> American Journal of Obstetrics, 1913, vol. lxviii, p. 649.

ligaments removed in the usual manner. The posterior peritoneum is then incised in a curved line with the convexity upward, running from one internal iliac artery to the other, and prolonged downward along the top of the broad ligaments, already divided in the preceding step. The internal iliacs are then ligated on each side in two places; after careful separation from the vein, the first ligation being placed just below the bifurcation of the common iliac, the second half an inch lower. With a large clamp, the artery is then crushed between them. In two instances the author was forced on account of an advanced atheromatous condition of the vessel, with beginning erosion due to softening of the glands at the bifurcation, to ligate the common iliacs, with no unfavorable results in either case. This procedure should be limited, however, to such unforeseen emergencies. If the uterine and obturator arteries can be ligated without cutting into carcinomatous tissue, this should be done, and one ligature must also be placed about the median sacral, if this is of sufficient size to require it.

The glands along the iliacs are then removed *en masse* if possible from the receptaculum chyli to the obturator foramen, as are also those situated within and around the latter. After such an operation, the uterus may be curetted or cauterized to a thin shell without danger of hemorrhage.

The operation is contra-indicated in the presence of extensive *cancerous* (not inflammatory) adhesions. The greatest danger is injury to the internal iliac vein, which lies just to the mesial side and behind the artery.

The author reports the results of 56 operations. Eight patients died within ten days; in 44, the symptoms were improved, and in 4 were completely relieved. In 35, the growth was retarded, in 11 the result in this respect was doubtful, in 9 negative. Hemorrhage, when present, was controlled in 39 cases, in 2 it was not controlled, but in these the bleeding consisted merely of a slight venous oozing and could not be called a real hemorrhage. All the patients who survived the immediate effects of operation were much more comfortable than similar ones not operated on, but treated identically in other respects.

**ARTERIAL LIGATION AND REMOVAL OF REGIONAL GLANDS.** The question which every surgeon should carefully consider before adopting any novel procedure is, Will the operation cure; if not, does it hold out a reasonable hope for alleviation of pain or distress. If one applies the query to the procedure which Bainbridge has adopted, he must be most skeptical as to its utility. We are forced to the conclusion after a review of his paper that he has really not alleviated the suffering of his patients by this intervention. We quote his article but cannot advise the adoption of his suggestion. In inoperable cases of cancer, palliative procedures are worse than useless, for they only act as a flare-back upon surgery and deter some poor individual from

seeking surgical aid, for the layman does not weigh these results from our view-point. Any operation performed for cancer which fails usually is looked upon as having actually hastened the end of the patient. No operation, therefore, which does not hold out a fair chance for cure or marked alleviation of suffering should be performed. An operation which is of questionable value in palliating symptoms, therefore, can serve no useful purpose, for it surely will retard the very movement in which we are all so actively involved, viz., our plea for early operative intervention.

**LIGATION OF ILIAC ARTERIES.** Green-Armytage<sup>1</sup> is also an advocate of ligating the internal iliac arteries as a palliative measure in cases of inoperable carcinoma of the cervix. His method is to ligate both internal iliacs a short distance from the bifurcation of the common iliac through a small incision in the peritoneum, and to ligate the ovarian arteries in the infundibulopelvic ligament. Then the patient is placed in the lithotomy position, and the uterine growth curetted and cauterized as in ordinary palliative operations; if her condition is not good at the end of the abdominal operation, however, this local treatment is deferred for ten days. The author believes that the comfort of the patient is much increased after this operation—in his experience pain disappears, discharge ceases, and the growth of the tumor is retarded for a time. In 4 of his cases, a marked vesical irritability which was present disappeared after operation. He says that in India, where he is working, many cases of inoperable carcinoma are seen in very young women—5 out of the 9 patients which form the basis of the present report having been *under thirty*, and one only twenty years of age.

**WERTHEIM'S RESULTS IN THE TREATMENT OF CARCINOMA CORPORIS UTERI.** An attempt has been made by Wertheim's first assistant, Weibel,<sup>2</sup> to tabulate and classify their results in cases of *carcinoma of the uterine body*, to which comparatively little attention has been paid in the past, on account of their relative infrequency and benignancy in comparison with those of cervical cancer. Although the figures of different observers vary considerably, the general opinion is that in about 5 per cent. of all cases of uterine carcinoma the disease involves the corpus, in the remainder the cervix being the part affected. Since practically all corpus cases are operable, whereas in the long run this can be said of not over 50 per cent. of the cervical ones, the proportion of fundal to cervical carcinomas *coming to operation* is about twice this figure, or 10 per cent. In the past fourteen years, Wertheim has seen about 1500 cervix, and only 70 corpus carcinomas. Of these latter, 2 were inoperable, and 1 refused operation, so that 67 were actually operated upon. While the number of cervix cases seen from year to year has remained practically constant, that of the corpus cases varies

<sup>1</sup> Indian Med. Gaz., 1913, vol. xlviii, p. 270.

<sup>2</sup> Arch. f. Gyn., 1913, vol. c, p. 135.

greatly, some years passing without a single one being seen, in others as many as 12 coming to operation.

The reason for the high operability of corpus carcinoma is to be found not only in the lack of parametric involvement—fixation of the uterus occurring only when the growth has extended through the entire wall, but also in the fact that this form of carcinoma occurs generally well after the change of life, the renewed bleeding thus reappearing after a more or less extended period of its absence, and being therefore noticed by the patient much sooner than is the mere irregularity or increased bleeding, occurring before complete cessation of the menses, which is usually associated with cervical carcinoma.

In the 67 operated cases, there occurred in addition to the corpus carcinoma, myomas in 19, ovarian cysts in 5, ovarian carcinoma in 4, ovarian sarcoma in 1, and tubal carcinoma in 1; in 10 of the cases the uterine carcinoma was found only by chance upon opening a uterus which had been extirpated for one of the above conditions. The frequent occurrence of ovarian carcinoma in this series is more than a coincidence, for the course of the lymphatics from the corpus to the ovaries explains the much greater frequency of the involvement of these secondary to fundal than to cervical carcinoma. The frequent combination of myomas with corpus carcinoma is also a matter of great importance. During the period of time covered by the report about 1000 myoma cases were operated upon, so that in almost 2 per cent. of these a corpus carcinoma was present as well, a matter of no small importance, Weibel thinks, when the question of palliative or  $\alpha$ -ray treatment of the former condition is to be considered.

The primary mortality in the 67 operated cases was 10.5 per cent. (7 deaths), these being distributed very unequally among the various types of operation. Thus of 16 patients operated upon by the *radical abdominal* method, 4 died; of 12 *simple abdominal panhysterectomies*, 2 died; of 3 *supravaginal amputations*, none died; and of 36 *vaginal extirpations*, 1 died. This mortality of over 10 per cent., practically equal to that now encountered in the radical abdominal operation for cervical cancer, is largely accounted for by the advanced age of most of the patients, this falling for the most part in the sixth decade of life, and being on the average considerably higher than that of the cervical cases.

One-fourth of the patients had never been pregnant, and 20 per cent. only once, these figures bearing out the general impression that corpus carcinoma occurs with much greater frequency among nulliparae than does cervical carcinoma.

Weibel does not share the general opinion that lymph nodes are seldom involved in corpus carcinoma. In the 31 laparotomies performed in the series under consideration, carcinomatous glands were found 5 times (16 per cent.), and as in some of the earlier cases no particular attempt

was made to find involved nodes, it seems not improbable that these figures should really be higher. The *inguinal* glands, however, were involved only in 2 cases, probably because of the small size of the lymphatics running along the round ligaments, the chief channels of transportation being (1) along the upper edge of the broad ligament to the ovary, then along the ovarian vessels, the common iliacs, and aorta, to the lumbar glands; (2) from the middle of the corpus, transversely through the broad ligaments to the iliac glands, at the bifurcation of the common iliac artery; and (3) along the walls of the tube. The most commonly affected glands are, therefore, the iliac and lumbar, exactly as is the case with cervical carcinoma. In some instances, the glands may show extensive metastatic involvement, while the parametrium is perfectly free.

Of the 60 cases which survived operation, recurrence took place in 19 (30 per cent.), almost invariably within the first year after operation; in 2 of these cases the recurrence was due, however, not to the uterine growth at all, but to a malignant adnexal condition (one ovarian sarcoma, and one primary ovarian carcinoma). Forty-three of the patients were operated upon more than five years ago; of these, 5 died from the operation, 16 had recurrences, and the remaining 22 are living and well, giving a five-year cure in 51 per cent. of operated cases, or an *absolute* cure of 50 per cent. Wertheim's cervical carcinoma cases, by his most recent compilation (450 cases traced five years or more since operation) show a cure in 42 per cent. of those *operated* upon, and a 20 per cent. *absolute cure*.<sup>1</sup>

With regard to the different operative methods, although the radical abdominal operation is associated with the greatest mortality, it also shows the highest percentage of cures, notwithstanding the fact that in this series it was used only in the more advanced cases. In view of this fact, and of the not infrequent involvement of the lymph glands, this method has now been adopted as a routine in the majority of instances at the Wertheim Clinic, though Weibel admits that not until a number of operators with extensive clinical material have taken up the subject of corpus carcinoma in the systematic way that cervical carcinoma has been attacked, can a definite judgment be formed as to the method of attaining the best results. For the present, he thinks that in every case the parametric connective tissue and regional glands should be removed and subjected to careful microscopic examination, in order to determine in just what proportion of cases they are involved. He also thinks that in every case of corpus carcinoma, no matter how operated upon, the adnexa should be removed, owing to the frequency with which they are involved.

<sup>1</sup> The "absolute cure" meaning, of course, the percentage of cases alive and well after five years in proportion to *all* that have applied for treatment, no matter whether operated upon or not.

## THE UTERUS.

**Radiotherapy of Myomas.** This question, which we discussed extensively last year, continues to occupy much attention in the German clinics, and numerous papers upon it have appeared in the continental literature. These have been for the most part, however, merely reports of results, quite favorable in some instances, less so in others, and have added nothing essential to the facts which we have previously brought out.

Krönig and Gauss, of Frieburg, continue to be the major prophets so far as this method of treatment is concerned; it cannot be denied that they have apparently developed the technique to a remarkable degree of perfection, and credit must be given them for an immense amount of exceedingly hard and painstaking work to put radiotherapy, especially *Röntgen* therapy, upon a thoroughly sound and scientific basis. Whether the ultimate judgment of the scientific world will uphold them in their extremely radical stand-point as to the lasting efficiency of this method of treating conditions such as uterine myomas, however, only time can tell. That they have not retracted in the least from this stand-point is shown by a recent article of Gauss,<sup>1</sup> who reiterates that the fundamental principles of successful *x-ray* therapy in gynecological work are, a short tube—skin distance, cross-fire, filtration (3 to 4 mm. of aluminum), and *very large doses*. He says that since his last report<sup>2</sup> fifty additional myoma cases have been treated, with no failures, although in some instances a total dosage of as high as 3000-X was required to produce a satisfactory result.

Since June, 1912, he has also been working with *mesothorium*, and has now a series of 150 patients treated in this manner for a large number of different conditions, among these being 79 cases of myoma and "metro-pathia." Of these, 29 have been completely cured, and 50 are still under treatment. The ages varied from twenty to sixty-four years. The myomas were of very different sizes, the largest reaching to above the umbilicus, but nearly all showed distinct shrinkage, and in some instances completely disappeared. No attention was paid to the amount of anemia in deciding for or against this kind of treatment, in some instances patients with as low as 15 per cent. of hemoglobin being successfully treated. In the majority of instances, amenorrhea was produced in about seven and one-third weeks, with two or three treatment-series. Occasionally unpleasant by-effects occurred, however, such as vertigo, vomiting, fever, pruritus, and in one instance thrombosis of the femoral veins.

Döderlein<sup>3</sup> is one of the few surgeons who have gone to the extent

<sup>1</sup> Strahlentherapie, 1913, vol. ii, p. 623.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1913, p. 224.

<sup>3</sup> Monatschr. f. Geb. u. Gyn., 1913, vol. xxxvii, p. 553.

advocated by Krönig and Gauss in the administration of massive *x*-ray doses, but he maintains that if the technique of the Freiburg Clinic is followed exactly in every detail, the same remarkable results as they claim can be obtained. He says that after much adjusting, under the personal direction of Dr. Gauss, he has finally gotten two *x*-ray machines working satisfactorily, and has now treated 21 myoma cases exactly according to the Freiburg method, with 100 per cent. of cures. He has found it possible by this technique to accomplish his purpose at *one sitting*; the great advantage of this lies not only in shortening the time necessary for treatment, but also in the fact that the much-feared period of increased bleeding, ordinarily resulting from the irritation of the first few exposures, is eliminated, and thus very anemic patients, whom one formerly did not dare to treat with *x*-rays, have become just the ones for whom it is particularly indicated. Döderlein would also remove from the list of contra-indications that of tumors (myomas) making pressure symptoms, even if causing retention of urine, for this can be temporarily relieved by means of the permanent catheter, and by giving sufficiently large *x*-ray doses, a shrinkage of the growth can be produced which will permanently relieve the symptoms, without resorting to operation.

AMERICAN REPORTS ON X-RAY TREATMENT OF MYOMAS. Notwithstanding the fact that Krönig and Gauss visited this country last fall, and presented papers summarizing their methods and results before the New York Academy of Medicine,<sup>1</sup> both our gynecologists and Röntgenologists appear to be possessed of a marked degree of skepticism with regard to the gynecological applications of radiotherapy; at least, reports of such work are chiefly conspicuous in the American literature by their absence. Among the few that have appeared, that of Pfahler,<sup>2</sup> of Philadelphia, is of considerable interest. He reports the results obtained in the *x*-ray treatment of 23 cases of uterine hemorrhage (21 of myomas, and 2 of "metropathia hemorrhagica"). He noticed in most instances a marked diminution in the size of the tumor, in addition to a reduction of the hemorrhage. In 12 out of 16 patients who have ceased treatment the tumor disappeared; in 2 of these the mass originally extended to the umbilicus, but after five and four years respectively it could no longer be found. The author has never seen a malignant degeneration of a myoma follow *x*-ray treatment, and does not think there is great danger of this. He does not advise applying this treatment to women under forty years of age; in treating very anemic patients, rest in bed should be insisted on after the first series of exposures, as the first applications of the rays are often followed by increased hemorrhage. In one case the treatment was followed by a temporary amenorrhea, with

<sup>1</sup> American Journal of Obstetrics, 1914, vol. lxix, p. 205.

<sup>2</sup> Ibid., 1913, vol. lxvii, p. 860.

disappearance of the tumor; then practically normal menstruation was reestablished, with recovery of perfect health.

Pfahler's method of procedure is to give the treatment in series of from three to nine applications, generally on successive days, with an intermission of about one month. If excessive bleeding has not ceased after six series, he considers the case unsuited for this form of therapy, and advises operative intervention. He uses filters of sole leather, plus an aluminum plate 1 mm. thick. One point which he emphasizes is that the cases should be carefully selected by a gynecologist, and treated by an expert Röntgenologist.

Stern,<sup>1</sup> of New York, also reports the results of *x*-ray treatment in 29 cases of uterine myomas, and 23 of menorrhagia and metrorrhagia. He says that while the number of treatments necessary to produce any improvement varies greatly, and in some instances no benefit whatever was seen, in the great majority of cases there was some improvement when the treatments were persisted in for several months, this usually amounting to a symptomatic cure so far as hemorrhage was concerned. In only 2 or 3 cases was there a tendency to recurrence of the trouble after stopping treatment.

*Technique.* Stern uses a type of filter quite different from that advocated by other Röntgenologists, namely, a layer of finely chopped ice, wrapped in absorbent cotton, and covered with a thin layer of rubber tissue. He thinks that this not only filters out the soft rays, but that also by chilling the skin it renders it less sensitive, and therefore less likely to develop a dermatitis. The dosage given is, according to continental standards, almost homeopathic—4-X at a sitting—the tube being placed at a distance of about 20 cm. from the skin, a little to the right and left of the median line alternately on different days. He regulates the frequency of treatment according to the severity of the case and what is to be accomplished, often dividing it into series of two or three sittings a week for six weeks, then intermitting for a time.

Unfortunately, the author is very vague in his statements as to his actual results, and does not indicate in any definite way the percentage of cases cured, improved, or not improved, nor in what class of cases he has had the best results.

A FRENCH OPINION ON RÖNTGEN THERAPY IN BENIGN UTERINE CONDITIONS. Siredey<sup>2</sup> has treated 59 patients suffering from uterine hemorrhage in the last three years, with no case of burn or accident. Three of the women became impatient and demanded operation, which was performed after they had received from eight to sixteen Röntgen treatments; in none of these was there the slightest interference with the healing of the abdominal wound, as might have been feared. Forty of the patients had myomas of various sizes, the remaining 19 had

<sup>1</sup> American Journal of Obstetrics, 1913, vol. lvii, p. 1133.

<sup>2</sup> Rev. de Gyn. et de Chir. Abdom., 1913, vol. xx, p. 113.

no true tumors, but sclerotic uteri with or without hypertrophy. Of the myoma patients, 2 were operated upon, 2 were still under treatment at the time of the report, and 1 had been given up as a failure. This was a woman, aged forty-one years, with severe cardiac disease, and a large myoma reaching to above the umbilicus. Owing to the cardiac condition, an operation was out of the question, and the *x*-rays were tried as a last resort, but with no benefit. All the remaining women, however, have received incontestable benefit from the treatment.

Siredey says that he does not care to use the word "cured," since all of these patients of course still retain their tumors, more or less reduced in size, but only the future can tell whether the relief will be permanent; at any rate, the menorrhagia, pain, symptoms of compression, etc., have disappeared, and the patients are able to resume their normal activities, in some instances entirely unrestricted, and in others with certain precautions.

Siredey is convinced that Röntgenization in these cases does more than merely to produce a "castration sèche," *i. e.*, elimination of ovarian function, but firmly believes that it also has a direct action on the tumors themselves, which results in a marked reduction in size, this differing greatly in degree in different individuals, but never going so far, in his experience, as to lead to the complete disappearance of a tumor of any considerable magnitude. In addition to the reduction of the exterior mass of the tumor, which can be demonstrated by abdominal palpation, Siredey has in a number of cases carried out careful measurements of the length of the uterine cavity, and has seen this decrease from 1.5 to 2 cm. within three months—too short a time, he thinks, for ovarian destruction to have been the cause.

His *technique* is briefly as follows: A dosage of 6-X is given over each of two skin areas at a sitting, through an aluminum filter 1 mm. thick. The sittings are given every seven days, unless reddening of the skin occurs, in which case an interval of two or three weeks is allowed to elapse. The time between periods of menorrhagia should be chosen for treatment as far as possible, but when these occur close together, Siredey has no hesitation in treating during the flow. The number of treatments necessary to secure the desired result varied in his experience from 9 to 40 and over in a few cases. Often the first period after treatment was increased, but by the third or fourth, great diminution was noticed, complete cessation following soon after.

SUMMARY OF GERMAN RESULTS FROM X-RAY TREATMENT IN VARIOUS CONDITIONS. Feeling that *x*-ray therapy, as applied to various gynecological affections, has now been practised long enough, and in a sufficient number of different clinics, to make a general stock-taking of its achievements of decided value, Mohr<sup>1</sup> has made an extensive tabulation, which

<sup>1</sup> Fortschr. a. d. Geb. d. Röntgenstr., 1913, vol. xx, p. 105.

includes all gynecological cases that he could collect to date from the German literature, which had been subjected to  $x$ -ray treatment, and concerning which sufficient data were given to permit of satisfactory classification as to diagnosis and result. In view of the enormously extensive literature which, as we have said, has already accumulated upon this subject, we feel that we cannot do better than to present here the more essential portions of Mohr's statistics, which show in a concise and easily comprehensible form just what has been accomplished in Germany with this form of treatment, practically from the time of its introduction up to the present.

#### I. MYOMAS (796 CASES).

At time of report there were:

|  | Cases. |
|--|--------|
| Still under treatment                      | 60     |
| Had withdrawn from treatment, uncured      | 27     |
| Nothing known concerning subsequent course | 40     |
|  | —      |
| To be eliminated, therefore                | 127    |

Of the remaining 669, there were:

Cured, 376 (56.2 per cent.); of these

|  | Cases.               |
|--|----------------------|
| Amenorrhea was produced in                     | 365 (97.1 per cent.) |
| Wished for oligorrhea was produced in          | 3 (0.8 per cent.)    |
| Cessation of pain (no menorrhagia) occurred in | 8 (2.1 per cent.)    |
|  | —                    |
| Total  | 376                  |

Improved, 120 (17.9 per cent.); of these

|  | Cases.              |
|--|---------------------|
| Amenorrhea was desired, oligorrhea produced in                           | 45 (37.5 per cent.) |
| Normal menstruation was produced in                                      | 13 (10.8 per cent.) |
| Improvement as far as hemorrhage concerned<br>(no further details given) | 62 (51.7 per cent.) |
|  | —                   |
| Total  | 120                 |

Improved and cured (no further details given)

|             | Cases.              |
|-------------|---------------------|
| Uncured     | 88 (13.2 per cent.) |
| Recurrences | 74 (11.1 per cent.) |
| Deaths      | 7 (1.0 per cent.)   |

(In one of these, there was severe anemia and dilatation of the heart, death followed a violent hemorrhage. In the other, death was due to heart weakness after improvement in the menorrhagia).

Treated for only a short time

|                           | Cured.      | Improved.  | Not cured. |
|---------------------------|-------------|------------|------------|
| 30 to 40 years, 28 cases  | 13 (46.4%)  | 12 (42.9%) | 3 (10.7%)  |
| 40 to 50 years, 131 cases | 161 (80.9%) | 13 (10.0%) | 12 (9.1%)  |
| Over 50 years, 43 cases   | 40 (93.8%)  | 2 (4.7%)   | 1 (2.3%)   |

## SIZE OF TUMOR (380 CASES).

|   |                      |
|---|----------------------|
| Remained unaltered in . . . . .   | 81 (21.3 per cent.)  |
| Was reduced in size in . . . . .  | 219 (57.6 per cent.) |
| Was markedly reduced in size in . . . . .                                 | 52 (13.7 per cent.)  |
| Entirely disappeared in . . . . .   | 20 ( 5.3 per cent.)  |
| Subjective feeling of diminution in size of abdomen occurred in . . . . . | 3 ( 0.8 per cent.)   |
| Increased in size in . . . . .  | 5 ( 1.3 per cent.)   |
| Total . . . . .   | 380                  |

## SEVERE HEMORRHAGE AT BEGINNING OF TREATMENT.

|  |        |
|--|--------|
| This was present in 23 cases; of these there were: | Cases. |
| Cured . . . . .                                    | 22     |
| Improved . . . . .                                 | 1      |

## ERYTHEMA DURING TREATMENT.

|                                       |        |
|---------------------------------------|--------|
| Occurred in 52 cases; of these it was | Cases. |
| Slight in . . . . .                   | 33     |
| Severe in . . . . .                   | 9      |
| Mere browning of skin in . . . . .    | 10     |

## NERVOUS SYMPTOMS OF ARTIFICIAL MENOPAUSE.

|                                |        |
|--------------------------------|--------|
| Occurred in 97 cases; of these | Cases. |
| Slight in . . . . .            | 85     |
| Severe in . . . . .            | 12     |

## VARIOUS DISTURBANCES DURING TREATMENT.

|   |  |
|---|--|
| Occurred in 24 cases.   |  |
| (Ischias, constipation, vomiting and diarrhea, vesical symptoms, nervous disturbances, rectal tenesmus, feeling of tension in breasts, reduction of libido sexualis.) |  |
|   |  |
|   |  |
|   |  |

## II. METROPATHIAS (354 CASES).

|   |        |
|---|--------|
| At time of report there were:   | Cases. |
| Still under treatment (in part somewhat improved)                                   | 39     |
| Had stopped treatment while still uncured . . . .                                   | 33     |
| Nothing known concerning subsequent course . . .                                    | 10     |
| Diagnosis of carcinoma made after short treatment and operation performed . . . . . | 1      |
| To be eliminated, therefore . . . . .   | 83     |

Of the remaining 271 cases, there were:

|   |                      |
|---|----------------------|
| Cured, 127 (46.8 per cent.); of these           | Cases.               |
| Amenorrhea was produced in . . . . .            | 119 (93.7 per cent.) |
| Wished for oligorrhea was produced in . . . . . | 8 ( 6.3 per cent.)   |
| Total . . . . .                                 | 127                  |

Improved, 32 (11.8 per cent.); of these:

|   |                     |
|---|---------------------|
| Amenorrhea was desired, oligorrhea produced in . . . . .                            | 19 (59.4 per cent.) |
| Normal menstruation was produced in . . . . .                                       | 6 (18.7 per cent.)  |
| Improvement so far as hemorrhage was concerned (no further details given) . . . . . | 7 (21.7 per cent.)  |
| Total . . . . .   | 32                  |

|                    |  |                     |
|--------------------|--|---------------------|
| Improved and cured |  | 79 (29.2 per cent.) |
| Uncured            |  | 28 (10.3 per cent.) |
| Recured            |  | 4 (1.5 per cent.)   |
| Died               |  | 1 (0.4 per cent.)   |

## AGE OF METROPATHIA PATIENTS (91 CASES).

|                          | Cured.     | Improved. | Not cured. |
|--------------------------|------------|-----------|------------|
| 20 to 30 years, 13 cases | 6 (46.2%)  | 1 (7.6%)  | 6 (46.2%)  |
| 30 to 40 years, 16 cases | 7 (43.8%)  | 4 (25.0%) | 5 (31.2%)  |
| 40 to 50 years, 50 cases | 35 (70.0%) | 8 (16.0%) | 7 (14.0%)  |
| Over 50 years, 12 cases  | 10 (83.4%) | 2 (16.6%) | —          |

## SEVERE HEMORRHAGE AT BEGINNING OF TREATMENT.

This was present in 6 cases; of these all were cured.

## ERYTHEMA DURING TREATMENT.

|                                       |        |
|---------------------------------------|--------|
| Occurred in 11 cases; of these it was | Cases. |
| Slight in                             | 5      |
| Severe in                             | 1      |
| Mere browning of the skin in          | 5      |

## NERVOUS SYMPTOMS OF ARTIFICIAL MENOPAUSE.

|                                |        |
|--------------------------------|--------|
| Occurred in 26 cases; of these | Cases. |
| Slight in                      | 24     |
| Severe in                      | 2      |

## IMPROVEMENT IN ASSOCIATED CONDITIONS.

During treatment, improvement was noted in some cases in the following symptoms: Leucorrhea, tachycardia, anemia, general weakness, nervousness, headache, hemoglobin percentage, weight.

Operation was subsequently performed in 15 cases.

## III. DYSMENORRHEA (19 CASES).

|  |                     |
|--|---------------------|
| Of these, there were:                  | Cases.              |
| Pregnant                               | 1                   |
| Nothing known as to subsequent course  | 1                   |
| To be eliminated, therefore            | 2                   |
| Of the remaining 17 cases, there were: | Cases.              |
| Cured                                  | 10 (58.8 per cent.) |
| Unimproved                             | 7 (41.2 per cent.)  |
| Total                                  | 17                  |

## AGE OF DYSMENORRHEA PATIENTS (9 CASES).

|                    | Cured. | Improved. | Unimproved. |
|--------------------|--------|-----------|-------------|
| 15 to 20 (1 case)  | 1      | ..        | ..          |
| 20 to 30 (3 cases) | 1      | ..        | 2           |
| 30 to 40 (1 case)  | ..     | ..        | 1           |
| 40 to 60 (4 cases) | 4      | ..        | ..          |

## IV. PRURITIS VULVÆ (30 CASES).

|                      | Cases.              |
|----------------------|---------------------|
| Cured . . . . .      | 18 (60.0 per cent.) |
| Improved . . . . .   | 3 (10.0 per cent.)  |
| Unimproved . . . . . | 9 (30.0 per cent.)  |
| Total . . . . .      | <hr/> 30            |

## V. KRAUROSIS VULVÆ (4 CASES).

|                           | Cases.  |
|---------------------------|---------|
| Cured . . . . .           | 0       |
| Unimproved . . . . .      | 3       |
| Under treatment . . . . . | 1       |
| Total . . . . .           | <hr/> 4 |

## VI. TUBERCULOSIS (13 CASES).

Divided into

|   |         |
|---|---------|
| Tuberculosis peritonei, 9 cases.  | Cases.  |
| Cured . . . . .   | 0       |
| Improved . . . . .  | 2       |
| (In both these cases, treatment with x-rays<br>was begun after a laparotomy had been<br>performed). |         |
| Died . . . . .  | 2       |
| Under treatment . . . . .   | 5       |
| Total . . . . .   | <hr/> 9 |

|  |         |
|--|---------|
| Tuberculous sinus in abdominal wall, 3 cases | Cases.  |
| Cured . . . . .                              | 2       |
| Markedly improved . . . . .                  | 1       |
| Total . . . . .                              | <hr/> 3 |

|                                     |       |
|-------------------------------------|-------|
| Tuberculous ulcer in vagina, 1 case | Case. |
| Cured . . . . .                     | 1     |

## VII. ADNEXAL DISEASE ASSOCIATED WITH HEMORRHAGE (10 CASES).

|  |          |
|--|----------|
| Comprised cases of:                      | Cases.   |
| Gonorrhea without adnexal mass . . . . . | 4        |
| Gonorrhea with adnexal mass . . . . .    | 5        |
| Puerperal tumor . . . . .                | 1        |
| Total . . . . .                          | <hr/> 10 |

Of these were:

|                                  |                    |
|----------------------------------|--------------------|
| Cured . . . . .                  | 5 (50.0 per cent.) |
| Amenorrhea produced in . . . . . | 2                  |
| Oligorrhea produced in . . . . . | 3                  |
| Improved . . . . .               | 2 (20.0 per cent.) |
| Under treatment . . . . .        | 3 (30.0 per cent.) |

Adnexal tumors disappeared in all cases.

Leucorrhea improved in all, but was cured in none.

Menopausal symptoms were severe.

## VIII. LEUCORRHEA (16 CASES).

Discharge stopped in all cases.

## IX. MALIGNANT CONDITIONS (53 CASES).

|   |        |
|---|--------|
| Inoperable cervical carcinoma   | 44     |
| Of these were:  | Cases. |
| Cured   | 0      |
| Pain was reduced in   | 43     |
| Discharge was reduced in  | 7      |
| No improvement in   | 1      |
| Prophylactic irradiation after radical operation                              | 4      |
| Under treatment   | 2      |
| No recurrence for periods of 8 and 14 months respectively                     | 2      |
| (Carcinomatous glands were removed from each of these patients at operation). |        |
|   | Cases. |
| Carcinoma of vulva  | 2      |
| Improvement in pain and discharge in  | 1      |
| No improvement in   | 1      |
| Carcinomatous glands  | 1      |
| Good result.  |        |
| Recurrence after operation  | 1      |
| Improved.   |        |
| Malignant peritoneal tumor  | 1      |

From the above recapitulation, it appears that something over half the cases of myoma have been considered by the attending surgeon as symptomatically cured, and an additional fifth or more as improved. There were only about 12 per cent. of the total number treated in which no improvement whatever is recorded. The rather low percentage of satisfactory "cures" reported is undoubtedly due to the large number of cases included which date from the earlier years of the use of radiotherapy before the technique was so highly developed as at present. On the other hand, in considering the comparatively small number of cases in which no improvement was noted, we must remember that the reports are for the most part from the pens of enthusiasts, whose judgment may have been in many instances—quite unconsciously no doubt, but none the less surely—tinged with optimism and enthusiasm. Moreover, since most reports of *x-ray* work are written shortly after the initial attainment of any given series of results, the table is of no value whatsoever in forming an estimate of the lasting value of radiotherapy versus surgery in these cases.

It is rather surprising to note that the percentage, both of cures and improvements, in the "metropathia" cases, *i. e.*, those suffering from uterine hemorrhage of indeterminable origin, without tumor—is distinctly lower than in the myoma cases, since it is particularly in the former field that *x-ray* therapy is generally believed to find its most important

application. Since the figures are gathered from a large number of observers, however, whose individual opinions as to just what constitutes cure or improvement may well vary within fairly wide limits, it would be unfair to attempt to draw any but the most general conclusions from the results as tabulated. These would certainly seem to indicate, in brief, that in well over one-half the cases of excessive, non-malignant uterine hemorrhage, whether or not associated with tumor formation, results satisfactory to physician and patient were attained by *x-ray* therapy, without recourse to surgical intervention.

Another point of some interest, brought out by the summary, is that while in a small proportion of the cases evidence of disturbances in the intestines, bladder, and other organs was seen, no serious injury to these, such as might be feared from the experimental investigations of Lacassagne and others, has been recorded.

**A Modified Type of Myomectomy Operation.** The ordinary myomectomy has the disadvantage that it does not permit a thorough examination of the uterus for small nodules which, when overlooked, may well lead to recurrences; moreover, after enucleation of a large tumor, it is often difficult to secure a satisfactory plastic reconstruction of the uterine wall. To obviate these difficulties, Freund<sup>1</sup> advocates the following operation, which he has been using for the last three years:

After opening the abdomen, and carefully palpating the uterus to see if the case is suitable at all for a conservation operation, he excises a large, wedge-shaped slice from the fundus and corpus, including both the anterior and posterior walls, and comprising all the tumor-bearing area. He starts by making a deep curved incision from a point in the midline of the posterior surface of the uterus, as low down as may be necessary, over the right side of the fundus to the middle of the anterior surface, at a point as low down as may be necessary. This cut should not involve the actual uterine horn or isthmus tubæ. This incision opens up the uterine cavity, but the hemorrhage is usually not great, and is easily controlled with clamps. Prying open the edges of the uterine incision, the operator now thoroughly palpates to determine if there are nodules in the portion of the uterus which is to be preserved, in which case, an ordinary hysterectomy is done. If not, a corresponding curved incision is made, starting and ending at the same points, but sweeping to the left, thus excising from the entire uterus a piece of tissue, shaped somewhat like a slice of melon, containing the entire tumor-bearing area, the size of the excised slice to be of course dependent upon the extent of this latter. After controlling the hemorrhage, and again thoroughly inspecting the remaining uterine tissue for tumor-nodules, the two halves are brought together by a double-tier suture as in the Sänger Cesarean section. As a rule, the walls are easily fitted together,

<sup>1</sup> Deut. med. Wochenschr., 1913, vol. lx, p. 1722.

the result being a reconstructed, functionally satisfactory uterus; care must be taken in applying the suture not to close the isthmus tubæ. The operation is neither long nor difficult, and the author has been greatly pleased with the results from it in the past three years.

**Lymphatic Supply of Myomas.** Polano<sup>1</sup> has made an interesting study of the lymphatics in 16 myomas by means of injection methods, using for this purpose a thin solution of camphor and coloring matter in ether. This mixture he injects by means of a very fine cannula directly into the tumor mass, with the idea of thus filling the finer lymph clefts, and from them the larger vessels. In some instances, the injection was made just beneath the capsule, in order to follow the course of the large vessels from it into the tumor, in others, the needle was thrust into the centre of the tumor, so that the fluid might be forced outward through the larger vessels toward the periphery, thus following the same direction as the normal lymph current. The specimens were then hardened for a few days in formalin, sectioned, and preserved in 50 per cent. alcohol.

Studied in this way, myomas appear to fall into two groups with regard to the lymph supply. In the case of single, "unicentric" nodules, there is, at one point of the circumference, a broad, pedicle-like connection between the tumor and the surrounding tissue, containing the lymphatic channels. In the much more frequent type of growth, however, composed of a conglomerate of smaller nodules, broad tissue bridges, carrying numerous lymphatic channels, are found at various points of the periphery connecting the tumor and capsule. In addition to these larger groups of vessels, there is found in both types of tumor an extremely fine canal system in the spiderweb-like tissue which is present between the tumor and the capsule throughout practically their entire extent. The lymph channels were specially rich and easily demonstrated in a few cases of lymphangiectatic tumors. Whether these arose as a result of true new formation of lymphatics, or merely from a dilatation of those already present, could not be determined, however. That simple dilatation probably plays an important role would seem to be indicated by the fact that lymphangiectatic changes are much more frequent in solitary nodules than in composite ones, a circumstance that could be well explained by the one area of efferent vessels in the one, as compared with numerous groups in the other.

The lymph-vessels do not appear to play a primary role in the production of necrosis in myomas, since in one specimen showing a distinct necrotic process there were multiple lymph connections to the surrounding tissue, without demonstrable occlusion. It seems probable, therefore, that necrosis depends upon a primary bloodvessel lesion, as a result of which toxins are formed in the myoma tissue, which are then

<sup>1</sup> Zeitschr. f. Geb. u. Gyn., 1913, vol. lxxv, p. 157.

by means of the lymphatics carried into the general system and produce clinical symptoms.

With regard to the anatomic relations of the lymph and bloodvessels, Polano found that while both systems are everywhere in most intimate relation to each other, no definite perivascular arrangement of the lymph spaces, such as occurs in some portions of the body, could be demonstrated.

**Effect of Myomas on the Blood Supply of the Uterus.** In continuation of the studies previously reported<sup>1</sup> upon the blood supply of myomas, Sampson<sup>2</sup> has been investigating by injection methods the effect produced by the presence of myomas upon the uterine circulation as a whole. He has found that small, *subserous myomas* (*i. e.*, tumors under 2.5 cm. in diameter) and also medium-sized ones (up to 10 cm.) do not disturb the circulation of the uterus, and do not alter menstruation. Larger subserous tumors may cause much enlargement of the branches of the uterine arteries from which they derive their nourishment, and also give rise to large venous channels in the pedicle and in the peripheral zone of the uterus, the normally somewhat anemic (at least with regard to the venous circulation) "radial zone" surrounding the uterine cavity remaining, however, unaffected. There is, therefore, no excessive escape of the venous blood into the uterine cavity, and the menstrual flow is not increased. Some of the large venous channels in the pedicle of these cases are very superficial, and are exposed to injury from the movements of the tumor, thus at times causing hemorrhage into the peritoneal cavity.

*Intramural myomas* do not apparently alter the arterial blood supply of the uterus as a whole to an appreciable extent, unless present in large numbers, when the uterine artery may be somewhat enlarged, and the plexus of veins in the myometrium may show about the tumors a localized or general dilatation, varying with their size. When the tumors are numerous there may also be an increase in the thickness of the uterine wall, due to actual hypertrophy of the myometrium, to dilatation of the venous plexus, or to both factors. Such tumors do not greatly interfere with the circulation of the uterus, however, and do not usually alter the character of menstruation, although they may indirectly cause menorrhagia or metrorrhagia, the factor of muscular insufficiency here playing a role.

Intramural myomas which encroach upon the uterine cavity cause an atrophy and anemia of the mucosa immediately over them; the remaining endometrium is usually hypertrophied, and its venous plexus is more dilated than normal. It is from this endometrium, and not from that encroached upon by the tumors, that the menstrual flow occurs. When excessive hemorrhage occurs in these cases, it is probably due

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1912, p. 182.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, 1913, vol. xvi, p. 144.

to failure of the uterine muscle to control properly this excessive amount of venous blood, and to a slow regeneration of the endometrium. Occasionally dilated veins in the endometrium directly over the tumor may become eroded and give rise to bleeding, but this is not very common.

*Submucous myomas* represent the later stage of the intramural variety, and the veins over their surface are more exposed to injury or degeneration than are those over intramural tumors, but even here the source of profuse menstruation is usually the endometrium not actually encroached on by the myoma.

**Nerves of the Uterus.** Comparatively few accurate studies of the finer nerve distributions within the uterine tissue have been made, probably owing to the great technical difficulty of satisfactorily demonstrating nerve filaments as distinguished from the connective-tissue fibrils, and the conclusions which have been arrived at by the few who have undertaken such investigations have been at quite marked variance. Of unusual interest, therefore, is some beautiful work reported during the past year by Hoogkammer,<sup>1</sup> who has used a technique quite different from that of most other investigators in this field. His method was to place freshly removed, still living ("überlebende") uteri in Ringer-Locke fluid at body temperature; the specimens were thoroughly injected with the same fluid under pressure, then with the same plus 0.1 per cent. methylene blue, and finally again with pure Ringer-Locke fluid, in order to wash out the excess of stain. Sections from the organs were then exposed to the action of oxygen for a time, since methylene-blue stains tissue best in a moist, oxygen-rich atmosphere. If the preparations then appeared sufficiently stained, the color was fixed with ammonium molybdate for twenty-four hours, followed by thorough washing; the tissue was then passed through ascending alcohols, and blocked in paraffin in the usual manner. A number of uteri from rabbits, calves, cats, and goats, two from adult women, one from a sixteen months' child, one from a newborn infant, and one from a seven months' fetus, were thus treated.

This method, while capable of giving very beautiful results, was found extremely uncertain, and often many preparations had to be made before satisfactory ones were obtained. Sometimes the methylene-blue stains the nerve tissue alone, at others it stains connective tissue, elastic tissue, muscle, epithelium, etc., every possible combination of two or more of these being seen in some of the preparations. The author found, however, that after one has learned positively to recognize nerve tissue from preparations in which this alone has taken the stain, preparations in which other tissues as well are colored are of great value in showing relations.

Hoogkammer found the entire uterine substance to be extremely

<sup>1</sup> Arch. f. Gyn., 1913, vol. xcix, p. 231.

richly supplied with nerves. These pass from the parametrium through the serosa into the myometrium, lying in the connective and elastic tissue, between the muscle fibers. Between the two chief muscle layers the larger nerve bundles divide, part continuing in a longitudinal, part in a circular course. The nerve bundles consist partly of medullated, partly of non-medullated fibers. Here and there very marked varicosities are met with along the course of the axis-cylinders. All the nerves, from the largest bundles to the smallest fibrils, show a distinctly spiral course, resembling often the tendrils of vines, an adaptation evidently to the variations in size of the uterus associated with pregnancy. In well-stained preparations, a wonderfully rich network of finest branches was found throughout the entire uterus, but the hypertrophy of pregnancy, of which other authors have spoken, was not demonstrable. In areas where apparently complete staining of the nervous system has taken place, every smooth muscle cell appears to be in relation with a delicate nerve, which ends *against* the protoplasm, never intracellular. Here and there in the endometrium, beautiful terminal arboration are found, such as have been described in the mucosa of other organs by Ranzier, Kölliker, and others. A very rich nerve supply is also found about all the bloodvessels, even the smallest capillaries showing at least one nerve fiber.

Three types of ganglion cells are found: (1) Small, bipolar cells, lying in the course of the smaller nerves, consisting of one neurit and one dendrit, and never grouped together into ganglia. These cells occur in all parts of the uterus; they have large nuclei, and but little protoplasm. (2) Large, round, often unipolar cells, lying in the course of the larger nerve bundles, and always grouped into smaller or larger ganglia. They are found in the parametrium, and in the outer layers of the musculature. With favorable staining and plane of section, a direct continuity between these and the nerve fibers can be plainly seen. (3) Richly branching, multipolar ganglion cells, with long continuations. These are found at times throughout the entire uterus, including the endometrium, and also in the ganglia mentioned under (2). Hoogkammer believes that these cells represent a true autonomic system, that they are independent nerve centres, which are of course in connection with the remaining nervous system, but which can activate the uterine musculature after all external connections are severed. This would explain the fact that an animal with a complete transverse lesion of the cord, or a woman with tabes or transverse myelitis, can pass through a normal labor, and that an extirpated uterus can undergo contractions in Ringer's solution.

**Menstrual and Inflammatory Changes of the Endometrium.** It is now over five years since Hitchman and Adler<sup>1</sup> published their original

<sup>1</sup> Monatssehr. f. Geb. u. Gyn., 1908, vol. xxvii.

painstaking and fundamental study of the endometrium, drawing attention to the cyclic changes normally occurring in it with each menstrual epoch, and emphasizing the fact that endometritis is a true *inflammation*, involving the *stroma*, and characterized chiefly by an invasion of small round cells. They now report<sup>1</sup> that further investigations have confirmed absolutely in their minds the correctness of this opinion. To objectors, who state that the changes described are not always regular, they say that the *premenstrual* changes are absolutely constant in cases with regular menstruation; the *post menstrual* and *interval* changes, however, are somewhat less so. They hold that the *premenstrual alteration of the endometrium to decidua-like tissue*, and not the production of hemorrhage, is the cardinal purpose of the whole menstrual process—the loss of blood is merely incidental. The papillary, secreting glands are the characteristic features of this stage; indeed, in some animals, although no bleeding occurs, exactly analogous changes in the endometrium have been found preceding rut.

The apparent discrepancies which occur between the histologic picture and the time of menstruation are practically all in cases with irregular menstruation, *i. e.*, with disturbances in ovarian activity. The characteristic gland formations begin to develop only six or seven days before the next period due, and do not reach their height until very shortly before its onset. It must also be remembered that different portions of the endometrium may be at the same time in a different stage; moreover, the *fundal region* is passive, and its endometrium does not participate in the characteristic histologic changes, so that in curettings, where bits from all regions are mixed, various pictures may be seen. Injuries to the endometrium incident to curetting must also be taken into account in interpreting the microscopic appearances. The *stroma changes* are much less constant and regular than the glandular, and are often to be seen only in the most superficial layers of the endometrium.

In cases of *irregular menstruation* the same general changes occur, but not in regular chronological order; the entire metamorphosis is compressed into a very short space of time, the individual phases often occurring not *after* one another, but all together, so that often in one field all stages of glandular development are to be seen, whence the mucosa acquires an indefinite character, from which no definite period in the cycle can be determined. Such atypical metamorphosis of the endometrium is no indication of any pathologic process in *it*, but rather of a disturbed functioning of the ovary. If this be true, then the old theory of irregular bleeding being due to *endometritis* must fall. Inflammation of the endometrium does not *per se* cause any disturbance of the regular cycle in the presence of normal ovarian activity (and therefore regular menstruation), nor does the presence of inflammation

<sup>1</sup> Arch. f. Gyn., 1913, c, p. 233.

in the endometrium cause a proliferation of the glands, as has been assumed.

For the microscopic diagnosis of *true endometritis* (*i. e.*, an actual *inflammation* of the uterine mucous membrane), no dependence can be placed on the bloodvessels and stroma, owing to the constant cyclic changes which are occurring in them, but reliance must be placed on the demonstration of an infiltration of round and plasma cells. The fresher the inflammatory process, the more pronounced is this infiltration of round cells, and the less the need for special staining; as the process becomes older, however, and the infiltration correspondingly less intense, the specific plasma cell stains become of greater importance. The authors' former dictum that "plasma cells are the absolute criterion of endometritis" must be somewhat modified, however, for while it is certainly true that their demonstration is the easiest way to diagnose it microscopically, if round cells can be definitely recognized by the ordinary methods, well and good.

The classical triad of clinical symptoms commonly associated with endometritis—irregular bleeding, pain, and discharge—must be given up; the only one of these that can be brought into a true causal relationship with the disease is *discharge*. Except in cases in which there exist purely mechanical causes, such as polyps, submucous tumors, carcinoma, etc., the authors believe that no change in the endometrium *itself* is ever directly productive of excessive or irregular hemorrhage. No matter what changes, inflammatory or otherwise, take place in the uterine mucosa, hemorrhage does not, in their opinion, result unless the *ovaries* are diseased; in other words, the cause of menorrhagia and metrorrhagia is never local in the uterus, except when due to one of the above-mentioned mechanical conditions. They would wipe off completely from our pathologic nomenclature the terms "hypertrophic" and "hyperplastic glandular endometritis;" the former term applies to a condition which is in no wise pathologic, but represents the normal premenstrual stage; the latter covers in part this also, in part variations in gland-richness within normal limits, and in part applies to conditions of real glandular hypertrophy of the uterine mucosa, which, however, have nothing to do with inflammation. Hitchman and Adler do not believe that hyperplasia and gland-richness of the endometrium have any etiologic connection with hemorrhage, nor do they believe that the character of such a mucosa is ever influenced by curettage, since it regenerates from portions that have not been removed, and assumes the same characteristics as it had before. That this is indeed the case is shown by the comparatively few instances of uterine hemorrhage that are permanently cured by curettage.

With regard to pain, the authors have observed so many cases in which a true endometritis has been present for a long time, without pain until other definite conditions have developed, such as parametritis,

perimetritis, or swelling of the adnexa, that they cannot bring the endometritis *per se* into any etiologic relation with this symptom.

There remains then, as the sole symptom of an *uncomplicated* endometritis, merely the purulent discharge from the uterus, a phenomenon which corresponds to the existing anatomic condition, namely, an exudation of inflammatory cells throughout the endometrial tissue. This exudate is to be clearly differentiated from the physiologic secretion of the glands, and also from desquamative catarrh of the vagina, a distinction which can easily be made with the microscope.

The authors believe that in the past far too much clinical importance has been attached to "endometritis;" not only has the mere existence of a discharge been credited with having an important influence on the general condition of the patient, but endometritis has been made responsible for every sort of pathologic condition. With regard to treatment, however, they have little to offer. They believe that, except in cases of endometritis occurring *postpartum* and *postabortum*, practically nothing is accomplished by curettage, since there is no more reason to suppose that a new, healthy endometrium will be produced after curetting away the major portion of a chronically infected one than when the same operation is performed for a condition of glandular hypertrophy. They consider, therefore, that curettage simply on account of discharge is never justifiable. For local applications, they favor formalin, on account of its germicidal action, and also because it coagulates albumin, causing necrosis and desquamation of the superficial tissue.

Very similar conclusions have been arrived at by Kjaegaard,<sup>1</sup> who has studied the endometrium from 211 patients, and has found essentially the same cyclic changes as those described by Hitchman and Adler. He divides the pathologic conditions which may occur in the endometrium into the following groups: (1) Endometritis chronica et subchronica; (2) hypertrophia irregularis glandularis; (3) subinvolutio mucosae menstrualis; (4) hyperplasia glandularis simplex; (5) polypus. In the second group, "*hypertrophia irregularis glandularis*," he places cases in which glands, which normally belong to different periods of the cycle, appear in various shapes, side by side, and gland projections are likewise found. The etiologic factor of this form is not inflammation, but must be looked for in other organs, especially the ovaries. The patients present a fairly constant symptom-complex: the hemorrhages are irregular, prolonged, and usually recur immediately after a curettage, or after a short period of amenorrhea. The condition occurs most frequently between the ages of thirty-five and forty-five; its diagnosis once made, treatment other than curettage is indicated.

<sup>1</sup> Kjobenh., 1913; (Internat. Abstr. Surg., September, 1913, p. 314).

*Subinvolutio mucosæ menstrualis* is characterized by a delay in the cyclic changes, so that the post-menstrual glands from one cycle are found alongside of the premenstrual ones of the next. These patients always have more or less prolonged irregular bleeding, and here, too, the etiologic factor lies probably in the ovaries rather than in the mucosa. Several of the author's cases of this type had no recurrence after curettage, whereas in others the abnormal bleeding soon recurred.

Kjaegaard places in the group of *hyperplasia glandularis simplex* those cases in which the mucosa is regular, and undergoes the normal cyclic changes, but in which there are quantitative variations from the normal; the borderline between normal and pathologic is drawn with much difficulty, however, in this group.

*Endometritis chronica et subchronica* is best diagnosed, he thinks, by the presence of plasma cells, though some cases can be recognized by the round-cell infiltration, without any plasma cells.

**Physiologic Studies of the Action of Various Drugs upon the Uterus.** In order to test the physiologic action on the uterine muscle of various oxytocic substances, Rubsammen and Kligermann<sup>1</sup> have made some forty experiments with strips of human uterus and human Fallopian tubes, obtained at operation, and placed immediately in Ringer solution. Tubes were used in many instances instead of actual uterine tissue, because while the tubal muscle is in every way analogous to the uterine, and shows practically identical reactions, the tube is less disturbed in its general relations by removal from the body than is a strip of muscle cut from the uterus, and when contraction of the musculature does occur, the shortening is more marked and more easily recognized.

When added to the Ringer solution in which the test pieces were suspended, *ergotin preparations* and *secacornin* actively stimulated the automatic contractions of the musculature; *suprarenin* was likewise found to be a powerful excitant, as were *hydrastin* and the *cotarnin preparations*; *hydrastis*, however, proved inconstant in action, as a rule inhibitory. In all cases, a thorough parallelism was found between the action of these drugs upon the human tissue with that upon animal tissues, as determined in a previous series of experiments.

Lieb<sup>2</sup> has also made numerous tests of a similar nature with the commonly employed ecbolic drugs, studying their effect on the blood pressure and auricular and ventricular action, when introduced intravenously into a narcotized dog, and also on isolated strips of guinea-pig uteri suspended in Ringer's solution. He has found that while *ergot* owes its physiologic action to several constituents, *ergotoxin* is the only one which is specific; each constituent, however, has a distinct pharmacologic action, stimulation of the uterus being a characteristic of them all, so that, at least in obstetric work, no single one of the

<sup>1</sup> Ztsch. f Geb. u. Gyn., 1912, vol. lxxii, p. 272.

<sup>2</sup> American Journal of Obstetrics, 1914, vol. lxix, p. 1.

active principles can replace preparations of whole ergot. Extracts of the posterior lobe of the *pituitary gland* stimulate all smooth muscle, while the anterior, glandular portion is apparently devoid of pharmacologic action, although essential to life. The active principle of pituitary extract has not been isolated, and it is not known whether the effects produced are brought about by one substance or by several. When added to Ringer's solution in the strength of 1 to 600 it causes the uterine muscle to contract very strongly, and to pass into tetanus, which is soon broken by incomplete relaxations.

*Quinin* also, in very weak solutions (1 to 100,000) causes an immediate increase in the rate and strength of uterine contractions, and when used in stronger concentration causes tetanus, followed by a fair degree of relaxation. When the concentration was made 1 to 25,000 the uterus was immediately thrown into spasm, a few minutes afterward showed signs of poisoning, and in a half hour was dead. The so-called "iso-quinolins" (*hydrastin*, *hydrastinin*, *narcotin*, *cotarnin*, etc.) all stimulate the uterine muscle directly, causing contraction of the organ as a whole, hence their value in menorrhagia and metrorrhagia. They do not affect the circulation, nor the coagulation time of the blood.

*Viburnum* was not tested very thoroughly, but appeared rather to stimulate than to quiet the uterus. Its action in dysmenorrhea, therefore, is probably due to a depression of the central nervous system, and not to a direct action upon the uterus.

Macht<sup>1</sup> has made a series of similar tests of the action of a number of the so-called emmenagogue oils on strips of pregnant and non-pregnant cat's uterus, suspended in Locke's fluid at 38° C., through which a constant stream of oxygen was kept bubbling. In such preparations, all reaction to manipulation has passed off in from fifteen to thirty minutes after the uterine tissue has been placed in the fluid; it then assumes a condition of almost complete relaxation, showing, however, small rhythmic contractions. These are recorded for a time on the kymograph, and then the drug to be tested is introduced into the chamber. Tests were made by Macht in this manner with *oleum hedeomae* (pennyroyal), *oleum sabinae* (savin), *oleum tanaceti* (tansy), *oleum rutae* (rue), *oleum thymi* (thyme), *oleum terebinthinae* (turpentine), and *apiol*.

None of these substances were found in any dose to have any stimulating action upon the uterus, but on the contrary they all caused its relaxation and even paralysis. The addition, e. g., of only 0.05 per cent. of pennyroyal to the solution immediately inhibited the powerful normal contractions of a pregnant uterus, and the same result was seen with tansy and apiole, these three drugs being apparently the most toxic of those examined, although all acted in a similar way, differing

<sup>1</sup> Journal of the American Medical Association, 1913, vol. lxi, p. 105.

only in degree. From these experiments, it is evident that the so-called emmenagogue oils have absolutely no stimulating effect on the uterus, but that on the contrary they inhibit its contractions and paralyze it. They, therefore, can have little if any therapeutic value, and if they have any action as abortifacients, such as is commonly attributed to them, it is probably no different from that of any other powerful systemic poison, such as phosphorus or arsenic. That they are by no means innocuous substances, however, is shown by a case reported by the author, in which death occurred four days after the patient, a sixteen-year-old girl, had taken thirty-six pennyroyal pills for the purpose of inducing abortion. An incomplete abortion was in fact brought on, but the patient succumbed; the chief lesions found at autopsy were fatty degeneration of the liver, kidneys, and heart, a patchy congestion of the ileum, and an edematous condition of the brain.

**Organotherapy.** PITUITARY AND OVARIAN PREPARATIONS. Bab<sup>1</sup> reports the treatment of 155 cases of uterine hemorrhage with *pituitrin*, the series comprising cases showing a large variety of etiologic conditions—uterine hypoplasia, hemorrhages of ovarian or thyreogenic origin without demonstrable genital lesions, inflammatory adnexal conditions, myomas, ovarian cysts, climacteric and luetic hemorrhages, etc. A complete cure was obtained in 81.2 per cent. Thirty-six other cases were treated for amenorrhea, with cure in 22; these patients were given *ovarian tablets*, subcutaneous injections of *ovarian extract*, *biorarium*, *thyreoidin*, and especially *aphrodisiacs* (*muiracithin*, *muira puama*, *damiana*, *yohimbin*, and *oöphorin-yohimbin-lecithin tablets*). The latter group of substances constitute, in the author's opinion, a valuable addition to organotherapeutics, as they cause hyperemia of the genital sphere, thereby stimulating the genital function and increasing internal secretions. In some cases, slightly unpleasant by-effects were noticed, such as pruritus, erotic dreams, epistaxis, headache, vertigo, and nausea.

Bab has also found these aphrodisiacs very efficient in the treatment of *sexual frigidity*, a condition which he thinks never exists except in association with definite developmental anomalies, such as hyper- and hypotrichosis, infantilism, metabolic and menstrual disturbances, etc. With preparations of the anterior lobe of pituitary, he was able to relieve post-climacteric disturbances, and both with these and with pineal extract to secure a marked hyperemia of the external genitalia, which suggested to him the use of these substances in the treatment of *kraurosis vulvæ*, but he has had the opportunity to try this in only one case so far; its use was followed by an alteration in the grayish-white appearance of the skin, and relief of severe pruritus of three years' standing, but further observation is necessary before the permanent value of this treatment can be determined.

<sup>1</sup> Frauenärzt., 1913, vol. xxviii, p. 543.

**EXTRACTS OF HUMAN OVARIES.** In a report presented at the International Congress in London, Recasens<sup>1</sup> advances the theory that extracts of *human ovaries* should be much more efficacious in treating disturbances due to hypofunction of these organs than extracts of ovaries obtained from animals, and especially should the ovaries of patients suffering with uterine myomas have a powerful action, for he considers the occurrence of tumors of this type due largely to an excessive activity of the internal secretion of the ovaries, a condition which is accompanied by a demonstrable hyperplasia of the interstitial cells of the stroma. Dysmenorrhea, on the other hand, is due, he believes, in at least one-third of the cases occurring in young women, to infantilism of the uterus, which is associated with deficient development of the ovaries. This is shown by the fact that in many of these women the menstrual disturbances disappear when regular sexual relations are instituted, resulting in a stimulation to ovarian development. In others, however, there is no change; the uterus remains infantile, the dysmenorrhea continues, and is here generally associated with sterility.

Acting upon the foregoing theoretic considerations, Recasens has tried in a few instances the therapeutic use of extracts from human ovaries removed during operations for uterine myomas. The patients from whom the material was obtained were under thirty-five years of age, and were healthy, aside from the presence of the tumor. Sterile extracts of these ovaries were put up in ampoules of 1 and 2 c.c., and were administered by hypodermic injection every third day for from one up to several months. Two cases of amenorrhea have been apparently cured, but in 2 others there was no result. Three cases of dysmenorrhea and oligomenorrhea were likewise cured; one of these subsequently became pregnant. Although these results are encouraging, the number of cases as yet treated is of course too small for the formation of any final judgment as to the efficacy of the treatment.

**EXPERIMENTAL STUDIES WITH PLACENTAL EXTRACTS.** The results of some experimental investigations along somewhat similar lines are presented by Aschner,<sup>2</sup> who has found that the injection of both *ovarian* and *placental extracts* into adult, virginal guinea-pigs produces not only the physiologic conditions regularly associated with rut—swelling and hyperemia of the uterus, ovary, and external genitalia, etc.—but may go on to produce a high degree of hematometra. These effects, however, are much more powerful with placental than with ovarian extracts. Also, the effects are less powerful in animals from whom the ovaries have been removed than in normal animals; it seems, therefore, that part (but not all) of the action of such extracts is due to the stimulation of the animals' own ovaries to increased activity. Aschner thinks that the violent uterine hemorrhage which is often associated with the pres-

<sup>1</sup> Zenttbl. f. d. ges. Gyn. sow. d. Grzgbte., 1913, vol. iii, p. 48.

<sup>2</sup> Arch. f. Gyn., 1913, vol. xcix, p. 535.

ence of a small placental rest may be due not so much to its presence mechanically preventing the proper contraction of the uterus, as to its internal secretory activity. He suggests therefore the trial, therapeutically, of placental extracts in the place of ovarian extracts; since the former could be made from human placentas they would have the great advantage of not being to so great a degree foreign to the body proteids as are extracts of animal ovaries.

**Prolapse of the Uterus.** That energy is still being expended in the attempt to devise new operations for the cure of procidentia is shown by the recent suggestion of a novel method of treating bad cases of uterine prolapse by free fascial transplantation, for which Schubert<sup>1</sup> stands sponsor.

**Technique.** The abdomen is opened either by the longitudinal or Pfannenstiel transverse incision, a strip of fascia, 1 cm. broad, being removed at the same time and placed temporarily in a sterile dish. The uterus is then drawn upward with a tenaculum, and a closed hemostat is forced through the mesosalpinx on each side close to the uterus; one end of the fascial strip is now drawn through one of these openings, the other end through the other. The central portion of the strip is fastened to the posterior wall of the uterus in the region of the attachment of the sacro-uterine ligaments (Fig. 102), and is covered, wherever possible, by a peritoneal fold formed from the posterior layer of the broad ligament (Fig. 103). The free, anterior ends of the fascial strip are now brought up through the abdominal wall in the same manner as they were carried through the broad ligaments, the recti muscles being punctured somewhat above the internal ring. On drawing upon these ends, the round ligaments are naturally thrown into plications, and are utilized for the peritonization of the fascial strips. After the peritoneum has been closed, the two fascial ends are overlapped and sutured together in a direction at right angles to the recti; the fascia is then closed over them.

Although the author has tried this operation as yet in but 6 cases, all of them too recent to judge of the lasting effect, he thinks it possesses such obvious advantages over those in general use that he wishes to place it before the profession for trial.

**SURGICAL IMPORTANCE OF THE UTEROSACRAL LIGAMENTS.** According to Somers and Blaisdell<sup>2</sup> there are really three kinds of tissue involved in these structures: (1) *muscle*, (2) *fibro-elastic tissue*, and (3) *peritoneal folds*. There has been in the past much confusion as to just what should be included and what excluded from the ligaments proper. In lower animals, the corresponding structures are rectovaginal, and not sacro-uterine. In all the animals examined (guinea-pig, Belgian hare, cat, dog, monkey) there is a distinct hypertrophy of the peritoneum over

<sup>1</sup> Zentbl. f. Gyn., 1914, vol. xxxviii, p. 21.

<sup>2</sup> Journal of the American Medical Association, 1913, vol. lxii, p. 1247.

the fold, this thickening being confined to the fibrous layer, within which are found a number of small trabeculae of unstriped muscle fibers,

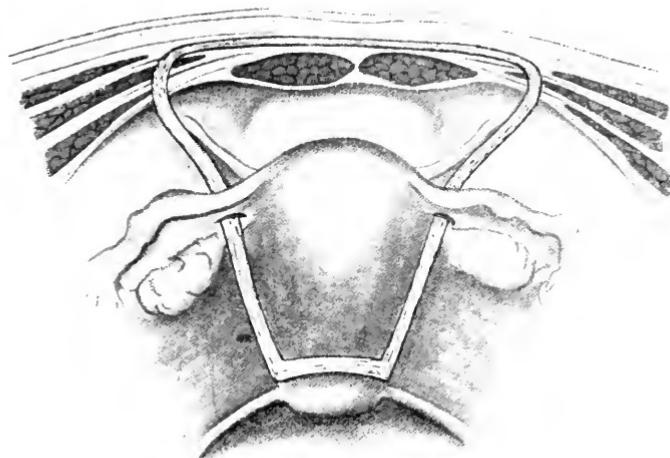


FIG. 102.—Relation of transplanted fascial band to the uterus, mesosalpinx, and abdominal musculature (schematic).

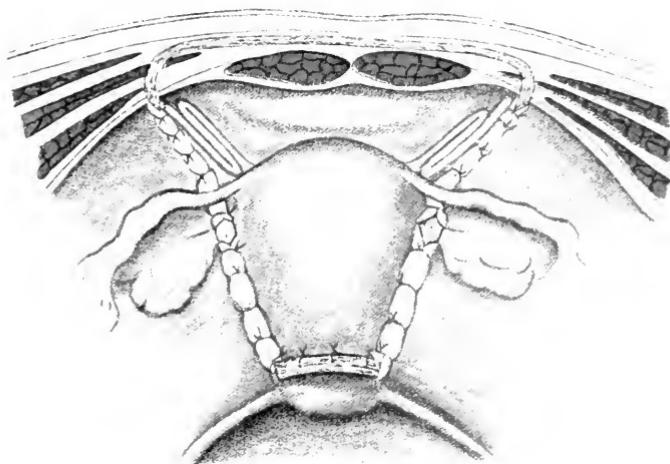


FIG. 103.—The fascial band has been covered with peritoneum, except where it crosses the lower uterine segment and the ovarian ligaments; in these situations, peritonization is impossible. The round ligaments are reduplicated, but no sutures have been placed.

these constituting a true recto-uterine muscle, since they originate from the uterus, pass first to the fold attached to the vagina, and then backward toward the rectum.

In woman, the sacro-uterine ligament is thicker and stronger than its homologue in animals, but consists of the same three parts. In some instances one or both folds are attached really to the rectum, in others both are attached to the sacrum. Beneath the plicae sacro-uterinae in the human female, filling all the space known as the parametrium, is a dense fibro-elastic network attached to the fascia of the levator ani below, to the obdurator fascia laterally, and to the peritoneum above. This tissue is practically absent in lower animals, appearing coincidently with the assumption of an upright position; it may be called the fibro-elastic suspensorium of the uterus. The sacro-uterine ligaments are merely a condensation of this meshwork, caused by traction. Interlaced with these fibers are fasciculi of smooth muscle, which by contracting and pulling on their attachments have the power of raising the uterus, evidently acting in this manner in response to reflex stimuli.

It seems highly probable to the authors, therefore, that these ligaments are of distinct surgical value. By making a circular incision about the cervix, as proposed by Jellet, and dissecting back the cuff of mucosa till the insertion is seen, the ligaments become easily accessible, and may be isolated by blunt dissection, and even cut away from the uterus if necessary. They may be doubled on themselves, sewed together, or severed and attached in a new position, as advocated by various authors. Somers and Blaisdell believe, as a result of these anatomic investigations, and of a small amount of operative experience, that the sacro-uterine ligaments are worthy of more general attention than they commonly receive, that the operation of shortening them is practicable and successful, and that it is particularly indicated when retroversion or prolapse is accompanied by a relaxed vaginal vault.

### THE OVARY.

**Radical Versus Conservative Ovarian Surgery.** The question of whether, in the long run, the best results are secured by pursuing a conservative or a radical policy with regard to the removal of all ovarian tissue, under certain conditions, from women before the menopause is one which it would seem may never be finally settled so long as two surgeons are left in the world to discuss it. Although the general trend of modern surgical opinion is unquestionably in favor of a rational degree of conservatism, especially in view of the increasing belief in the importance of the ovary as a gland of internal secretion, there are not wanting those who consider the supposed benefits to be derived from preserving some ovarian tissue wherever possible chimerical and imaginative. Firmly believing, as we do, that in the vast majority of cases the best interests of the patient are served by preserving an ovary, or even a portion of one, even if all possibility of pregnancy is irrevocably lost,

we feel that it is only fair that those who favor rather the radical policy should have a hearing.

Graves,<sup>1</sup> for instance, has attempted by means of a questionnaire to ascertain to what extent deleterious effects can be traced to the removal of all ovarian tissue. For this purpose he has sent out letters with the following questions to a series of patients who had undergone supravaginal hysterectomy with the removal of both ovaries, each patient being asked: (1) Whether or not she had suffered from hot flashes. (2) Whether she had been more nervous or less nervous since the operation. (3) Whether she had had any change in sexual feelings. (4) Whether or not she considered herself improved in health by the operation, and to what extent. In a few of these patients there had been an attempt at implantation of ovarian tissue, but in the majority this had been entirely removed.

Of the 136 women who answered, 60 had suffered from hot flashes for a few months, 42 had had them slightly, but were not seriously troubled, and 28 had not noticed them at all. Ninety-six reported that they were less nervous than before, while 40 reported either that they were the same or more nervous; of these, 33 said that their general health had been improved, and in no case was there a definite, severe psychoneurosis directly traceable to loss of ovarian secretion. Only 101 women answered the question regarding the changes in sexual sensibility; of these, 72 reported no change, 5 said that desire and sensation were stronger, 18 that they were diminished, and 6 simply said "changed," without specifying. A few complained that coitus was painful since operation, and others that it had been painful before operation, but had ceased to be so since.

In those cases where hot flashes and nervous symptoms do occur, the author has found the administration of ovarian extract of very marked benefit, and now adopts this treatment routinely after hysterectomy if hot flashes are complained of, though in other gynecologic conditions he has found it of very doubtful value.

As a result of these answers, he concludes that the preservation of ovarian tissue is not a matter of very vital importance.

A strong plea against conservative surgery in dealing with practically all kinds of *ovarian neoplasms* is made by Silhol.<sup>2</sup> He advocates, in all cases where one ovary has to be removed on account of a cyst or any kind of tumor, no matter how benign its appearance, that the other ovary should be removed as well, basing this opinion upon the following argument:

Ovarian affections are known to possess a great tendency to bilaterality; this is as true of microcystic degeneration as of true neoplasms, but is of course specially true of malignant growths. Although many

<sup>1</sup> American Journal of Obstetrics, 1913, vol. lxvii, p. 649.

<sup>2</sup> Arch. mén. d'Obstet. et de Gyn., 1913, vol. iii, p. 338.

authors have considered the bilateral occurrence of these often a sign of secondary origin from some primary origin in the digestive tract, this is certainly in many instances not the case. It has been demonstrated beyond doubt that malignant tumors of the ovary can frequently cause metastasis in the tubes, uterus, or other ovary. Silhol claims that everything which has been said with regard to malignant tumors applies with equal force, however, to ovarian cysts, for the most innocent appearing cyst may act in every way like the most malignant tumor. This is illustrated by two cases observed by him, in which two and one-half and three years respectively after the removal of an apparently benign ovarian cyst from one side, the patient returned with a recurrence in the other ovary, leading in one instance to death a short time afterward. Notwithstanding the fact that in many instances the remaining ovary remains entirely healthy after unilateral oophorectomy for a cyst, he does not consider the risk worth taking, but thinks that in all cases of tumor involving one ovary, the other should be invariably removed.

This stand-point certainly appears unnecessarily radical, since in many instances of unilateral benign ovarian neoplasm, such as multilocular or simple cyst, dermoid, etc., to remove the healthy ovary also is not only to deprive the woman of whatever internal secretory function that organ may possess, but of fecundity as well, for in conditions of this character the reproductive power is generally not lost, as is the case after hysterectomy, and almost always in advanced inflammatory lesions. Completely to unsex a young woman, and to deprive her of all hope of offspring, because of the remote possibility of a malignant condition subsequently developing in a sound ovary, in the presence of an undoubtedly benign neoplasm of the opposite organ, requiring its removal, seems from our stand-point at least, utterly unjustifiable. Even should trouble subsequently develop in the ovary not removed, necessitating a second operation, such a condition is rarely malignant, at least at first; in view of this fact, and of the comparatively small number of cases in which it occurs at all, the risk certainly seems well worth the price. Of course, if the original unilateral lesion shows the least suspicion of *malignancy*, the question assumes a different aspect at once, this only emphasizing, however, the great importance, especially in ovarian surgery, of a thorough knowledge of "living pathology" on the part of the operator.

**Ovarian Transplantation.** One of the most constant experimenters with the *transplantation of ovarian tissue* in the human subject is Tuffier,<sup>1</sup> who has been practising it for a number of years, and believes that it furnishes the best solution of the problem of ovarian conservation in certain cases. He says that in operating on pelvic inflammatory

<sup>1</sup> Jour. de Chir., 1913, vol. x, p. 529.

disease in young women, when the removal of both tubes and ovaries is indicated, he always leaves the uterus if possible. After removing the adnexa, he separates the ovaries from the tubal mass, and inserts them into the subperitoneal cellular tissue on each side, at a distance of about 5 cm. from the peritoneal incision, spreading the cut surface as much as possible over the surface of the aponeurosis. He has found that practically any ovary, no matter if "sclerocystic," is useful as a graft, provided it is aseptic. No sutures are used to hold the implanted ovaries in place, the abdominal wall merely being closed in the usual manner.

In bad inflammatory cases, the author considers this process preferable to merely leaving the ovaries in place and removing only the tubes, since if this is done, the ovaries are liable to become painful and require the performance of a second laparotomy, whereas if the transplanted organs give any subsequent trouble, a simple incision through the abdominal muscle, under local anesthesia, is sufficient for their removal.

Tuffier has done 44 operations of this type in the past six years, and has kept track of 19 of the patients, in 14 of these eleven months or more having elapsed since the operation. In all but one instance the menstrual flow has been maintained, but in all cases there was an interval varying from three to seven months after operation before menstruation was reestablished. Each period is preceded from three to ten days by a distinct swelling of one or the other ovary, which can be easily felt beneath the abdominal wall. Only one ovary appears to be affected at each period; with the appearance of the flow the tumefaction disappears, and in the intermenstruum the ovaries are scarcely demonstrable. Sometimes it is the organ on one side, sometimes the other, which shows the premenstrual swelling, but there does not appear to be any regular alternation in this respect.

In one instance, menstruation is known to have been regularly maintained for over five years, and several other patients have been followed for over two years with the same result. In 2 patients the engrafted ovaries were subsequently removed (in one instance after three and one-half years); not only could the presence of newly formed arteries and veins of good size be demonstrated entering the periphery from the surrounding tissues, but histologic examination showed the presence of corpora lutea, indicating that actual functioning had taken place.

In none of the patients have the symptoms of the artificial menopause—hot flashes, etc.—persisted after the reestablishment of menstruation, although in some instances they were noticed in the interval between the operation and reappearance of the flow. From this fact, Tuffier concludes that the menopausal disturbances are due rather to a *suppression of the normal regular recurring loss of the menstrual blood* than to suppression of the ovarian secretion *per se*, a conclusion which appears to him further strengthened by the fact that in cases where the

uterus was removed and the ovaries grafted, these symptoms occurred as after ordinary castration.

*Ultimate Results.* Of the 14 cases followed for eleven months or more, 2 have had regular, normal menstruation; 2, irregular menstruation and several attacks of menorrhagia; 4 have had irregular menstruation; 3 menstruated for about two years, and then gradually became amenorrheic; 1 has had extremely prolonged periods amounting to menorrhagia; 4 have had some pain in the region of the uterus or of the grafts, necessitating in 2 cases the removal of the latter. It would seem, therefore, that while in some instances the engrafted ovary becomes a normally functioning organ in its new situation, in other cases, proper nutrition is not established, and atrophy occurs, a condition which it is hoped further development of the technique will remedy. It seems probable that with further experimentation, more definite indications and contra-indications for the operation will be established; at present Tuffier does not advise performing it on any woman over forty years of age, as in no such case has he seen menstruation maintained.

Whitehouse<sup>1</sup> reports a single case of autoplasic ovarian transplantation, performed upon a woman on whom he operated for pelvic inflammatory disease, the lesions being so extensive that no ordinary type of ovarian conservation could be considered. The right ovary contained a corpus luteum abscess, the size of a small orange, and was completely adherent to the corresponding tube, the left ovary was firmly bound down behind the left tube, and the uterus was surrounded by adhesions, but appeared otherwise healthy, and was left *in situ*. Both adnexa were removed, and the healthy portion of the left ovary was then chopped into small pieces, which were scattered throughout the subperitoneal connective tissue under the rectus muscle.

The patient has been followed for a year since operation, which has so far apparently been entirely successful; menstruation gradually disappeared, sexual feeling has not been diminished, and no dyspareunia has occurred. The author thinks that this method of chopping up the ovarian tissue to be implanted is superior to that of using a large piece of an entire ovary, as the smaller bits are more easily nourished; he emphasizes the importance of leaving the ovarian tissue in place till the last possible moment, and then transplanting it as quickly as possible, in order that it may not be deprived of contact with the body fluids for any considerable length of time.

### THE FALLOPIAN TUBES.

**Treatment of Salpingitis.** Stone<sup>2</sup> advocates the following treatment in cases of *subacute salpingitis*: The patient is anesthetized, the cervix

<sup>1</sup> British Medical Journal, 1913, No. 2752, p. 783.

<sup>2</sup> Journal of the American Medical Association, 1913, vol. lx, p. 656.

dilated, and a blunt curette used if thought necessary. By means of a glass syringe having a conical point long enough to reach through the internal os, a solution of *one part tincture of iodin to three parts of alcohol* is injected into the uterine cavity, strong pressure being made on the piston of the syringe, and maintained for at least two minutes, so as thoroughly to dilate the uterine cavity. The abdomen is now opened, the tubes are freed from any adhesions, and irrigated with the same solution injected from the abdominal end. The subsequent surgical proceedings are as conservative as possible, a tube or part of a tube being retained if possible. In many cases, it is found on opening the abdomen that the iodin has been forced into the tubes from the uterine injection, but this is not always the case, and therefore the author considers injection from the abdominal end necessary as well. He believes that this method assures a thorough sterilization of the tubal and uterine mucosa, and offers the best opportunity for a *restitutio ad integrum*, but is not able to report any definite results in the support of this assumption.

A somewhat similar method of treating this class of cases is described by Lörincz,<sup>1</sup> who injects into the uterus a 2 per cent. solution of *argentamin*. He makes no attempt to use pressure, or to dilate the uterine cavity, but on the other hand, insists that the cervical canal must be sufficiently dilated to permit of the fluid flowing out easily. Absolute rest in bed must be maintained throughout the treatment, which lasts as a rule from five to six weeks, from 25 to 40 injections being given during this time. If improvement does not occur after a trial of the method for this period, it should be abandoned in favor of operation.

**Causal Relationship between Cervical Tears and Salpingitis.** The theory that cervical lacerations may be an etiologic factor in the production of certain forms of salpingitis is advanced by Reder,<sup>2</sup> who calls attention to the fact that often during a laparotomy for some other condition, an unsuspected salpingitis is discovered, which either had given no symptoms, or whose symptoms were overshadowed by the major condition. The inflammation is of low grade, the tubes—for the condition is invariably bilateral—are somewhat swollen, of a dull, reddish hue, but quite free, and often prolapsed. In some instances the abdominal ostium is closed, with the formation of a small hydro-salpinx. The author says he has never found this type of tubal disease in a woman who had not borne children, and believes that it results from an ascending infection of low grade.

Microorganisms, such as streptococci, staphylococci, and colon bacilli are constantly found about the vulva; in the non-parous woman the resisting powers of the vagina and cervix are sufficient to prevent an entrance of these into the deeper tissues, but if the cervix has been

<sup>1</sup> Gyògyászat, 1913, vol. liii, p. 40 (Internat. Abstr. Surg., June, 1913, p. 542).

<sup>2</sup> American Journal of Obstetrics, 1913, vol. lxviii, p. 902.

torn, with a resulting eversion and chronic inflammatory condition of the lips, it has a distinctly lowered resisting tone, and through its rich lymphatic supply invites an acute microbic invasion. From the cervix, the infection may easily travel to the tubes and broad ligaments. That this mode of infection actually takes place is shown, the author thinks, by the frequency with which cervical lacerations are found in conjunction with such tubes, and by the fact that after plastic operations on the cervix, restoration of the tubes apparently takes place. Often such patients, who have passed through a long period of sterility, will become pregnant after suitable plastic procedures, even if the tubal ostia have been found apparently closed at the time of operation. In Reder's opinion, therefore, such tubes should in no case be removed, but the fimbriated ends should be freed, the mucosa turned back and retained with a suture, and the primary focus obliterated by repair of the lacerated cervix.

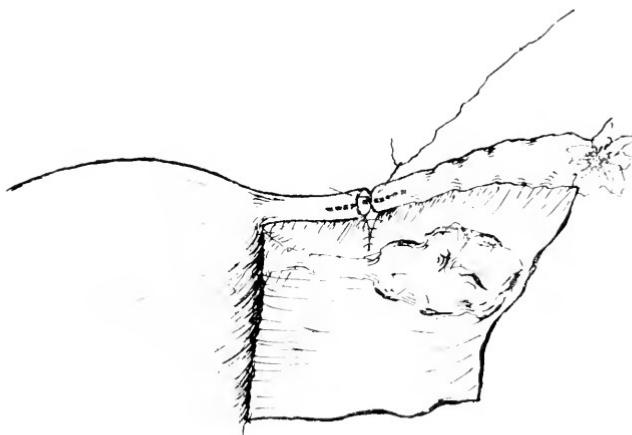


FIG. 104

**Technique of Anastomosis of an Occluded Tube.** A method of dealing with the rather rare condition of an interruption at some point of the continuity of the tube-lumen, the two ends being, however, apparently functionally intact, is suggested by Christian and Sanderson.<sup>1</sup> If for any reason the tube has been cut through, simple end-to-end apposition with suture generally leads to obliteration of the lumen at that point, with consequent loss of function. To obviate this, the authors suggest inserting a piece of No. 0, twenty-day catgut, for about three-eighths of an inch into each end of the tube, the two ends being then brought together with two apposing catgut sutures (Fig. 104). The lumen cannot now become obliterated during healing of the divided ends, owing to

<sup>1</sup> Journal of the American Medical Association, 1913, vol. lxi, p. 2157.

the presence of the catgut, which remains until the reparative process is complete, eventually, however, undergoing absorption, and being completely removed.

The application of this method was shown in a case reported by the authors, in which the left adnexa had been removed at a previous operation. The patient was operated upon a second time for the removal of a small hemorrhagic cyst of the right ovary; at the same time a piece half an inch long was resected from the middle third of the right tube, as it was constricted from previous inflammation, and proved to have an obliterated lumen. The cut ends were joined in the manner described above, and the patient has since become pregnant.

**Treatment of Sterility by Tubal Dilatation.** A method of treating certain cases of sterility, in which the trouble is apparently due to stricture in the course of the tube, is described by Lewis,<sup>1</sup> who reports two instances in which he has performed a dilatation of the Fallopian tubes for this purpose. The first case was that of a nullipara, married five years, upon whom an operation for appendicitis was necessary. During the operation, inspection showed the uterus and ovaries to be apparently normal, but the tubes were stenosed. They were dilated from the ostium to the uterus, and within eighteen months the patient was delivered of a normal child, having since then passed through a second pregnancy.

The second case was a woman, aged thirty years, married four years, and sterile. A dilatation, curettage, and decision operation had been performed about one year after marriage, without any result. In addition to the sterility, the patient suffered with severe pains for about three days just about midway between the periods (the so-called "Mittelschmerz" of the Germans). In this instance, Lewis opened the abdomen with the deliberate intention of dilating the Fallopian tubes; both of these were found to contain a number of strictured areas, and were, with some difficulty, thoroughly dilated by passing probes of gradually increasing size well up into the uterine end. The first effect was the disappearance of the pain between the periods, and less than two years after operation the patient was delivered of a healthy child.

**Tubal Sterilization and Interruption of Pregnancy.** Under certain conditions, such, for instance, as the presence in a married woman, pregnant in the early months, of an active tuberculous lesion, or of some grave constitutional condition, which would place her life in jeopardy were the gestation permitted to continue, it may be necessary not only to interrupt the existing pregnancy, but to prevent the possibility of future conception. Since patients of this class are at best poor operative risks, it becomes at times highly desirable to accomplish both these results at one sitting if possible. Among the various methods of

<sup>1</sup> British Medical Journal, 1913, No. 2741, p. 70.

doing this which have been devised, that suggested by Hoffmann<sup>1</sup> appears to possess to a high degree the qualities of simplicity and efficiency.

His technique is to make a median incision; the pregnant uterus is drawn forward as far as possible and opened in the median line for a sufficient distance to permit the extraction of the products of gestation. The uterine cavity is then thoroughly curetted through the incision to remove all decidua, and is closed with three running catgut sutures. The tubes are ligated about 1 to 2 cm. from the uterine cornu, and the stumps buried between the layers of the broad ligament with running silk sutures. At the beginning of the operation 1 c.c. each of secacornin and pituitrin are given by intramuscular injection.

The advantages claimed by Hoffmann for this operation are absolute asepsis, easy control of hemorrhage, certainty of producing sterility, and the short time necessary to perform it.

**Toxicity of Blood in Peritoneal Cavity after Tubal Rupture.** Els<sup>2</sup> strongly urges that every bit of *free blood* should be removed from the abdominal cavity after a ruptured tubal pregnancy, believing that this blood has very definite toxic qualities, as a result of which its absorption may cause serious harm to the maternal organism. He thinks that in the majority of cases of ectopic gestation which die, not at the time of operation or within a few hours, but within the next few days, death is due not to the hemorrhage itself, but to the toxic effects of blood which at the time of operation has been left in the abdominal cavity and is subsequently absorbed. This blood, found in the abdominal cavity after a ruptured tubal pregnancy, differs in two important points from that found after any other intra-abdominal catastrophe, such as laceration of the liver, spleen, or kidney, in that it possesses much greater toxicity, and remains much longer unclotted.

The first of these properties, its toxicity, the author believes to be due to a form of anaphylaxis. It is known that fetal protein is of sufficiently different constitution from maternal protein for the former to cause severe toxic symptoms when introduced in sufficient quantities into the maternal organism. Thus, eclampsia is believed by many to be merely an anaphylactic phenomenon, caused by the entrance into the maternal circulation of an excessive quantity of fetal proteins. When tubal rupture occurs, the chorionic tissue is lacerated, and a considerable quantity of fetal protein is mingled with the escaping blood. The maternal organism, previously "sensitized" by the gradual absorption of minute quantities of fetal products, is now overwhelmed by the rapid absorption from the peritoneum of large amounts of these with the non-coagulated blood which has been poured out—the ideal condition for the production of a severe state of "anaphylactic shock."

<sup>1</sup> Zeitschr. f. Geb. u. Gyn., 1913, vol. lxxv, p. 320.

<sup>2</sup> Arch. f. Gyn., 1913, xcix, 167.

The greatly lengthened coagulation time of this blood is explained by the author as follows: The smooth, endothelial-lined walls of the abdominal cavity and contained viscera, together with the maintenance of body temperature, do not of themselves favor coagulation of the blood. In the case of a rupture of one of the abdominal organs other than the pregnant tube, however, a comparatively large wound surface is left. Clotting is greatly hastened, as is well known, by contact of the extravasated blood with a fresh wound surface, since such a surface, and especially the lacerated vessel walls contained in it, are continually giving off thrombokinase, which is necessary to the process of coagulation. In tubal rupture, however, an extensive hemorrhage may occur from a very tiny area of injury; there is but little wound surface, or injured vessel wall surface, to give off coagulation-furthering ferment, and the blood remains liquid for a long time, hence favoring rapid and extensive absorption from the peritoneal surface. In the case of hematocoele-formation, however, which generally occurs with *tubal abortion*, only a small amount of blood is exuded at a time, usually into the tubelumen, where it coagulates, and is then forced out by succeeding hemorrhages into the abdominal cavity, very little uncoagulated blood thus reaching the latter at all; absorption, therefore, is slight, and toxic phenomena are correspondingly unimportant.

The author advocates in all cases of ruptured tubal pregnancy immediate operation, ligation, and removal of the affected tube, and then careful swabbing out, with a stalked sponge, of all blood from the abdomen, the head of the table being raised high during this procedure, so as to let the blood run down into the small pelvis as far as possible.

While much of what Els says in the foregoing article is undoubtedly sound, we cannot help feeling that he goes somewhat too far in advocating this extensive peritoneal toilet in *all* cases of ruptured tubal pregnancy with free blood in the abdomen. Many of these patients are in such bad condition at operation that anything which would prolong this for a moment beyond the time absolutely necessary to control hemorrhage and remove the affected tube would add seriously to the risk, certainly much more than would be compensated for by the assurance that we had obviated all possibility of the subsequent development of a condition of anaphylactic shock. The idea, moreover, that eclampsia is an anaphylactic phenomenon rests much more on a foundation of theory than of demonstrated fact, no really conclusive data in support of this conception having been as yet brought forward. It would seem, therefore, that while it may be highly desirable thoroughly to free the peritoneal cavity from blood in operating for ruptured tubal pregnancy, when the patient's condition is such as to permit of doing this without adding materially to the risk of the operation, it would be a dangerous doctrine to insist upon doing this in all cases.

### THE LOWER GENITAL TRACT.

**Gangrene of the External Genitalia.** About 40 cases are on record of a condition in the male which Fournier called "fulminant gangrene of the genital organs," but up to the present time, only 2 cases have been described in women. Those studied in the male sex were always found in young, vigorous subjects, without hereditary taint. Some authors have considered alcohol, others sexual excesses as the cause, but the etiology has never been definitely determined.

Spillmann, Thiry, and Benech<sup>1</sup> report a case of this unusual and most serious condition occurring in a young girl of eighteen years, who applied for treatment on account of a gangrenous area involving the labia majora, groins, and anal region, reaching to the sacrum. The only history obtainable was that the condition came on after an attack of diarrhea. The peritoneal muscles appeared completely dissected; an intense, putrid odor was given off in spite of frequent dressings, and the patient soon developed a high temperature, with all the symptoms of severe systemic infection. The necrotic process advanced steadily, and within ten days a great cloaca had formed in place of the vagina and rectum. Two injections of neosalvarsan were given, and were followed by a temporary fall in the temperature, but no other benefit was produced. On the twelfth day, a two-months' fetus was expelled; soon after this, decubital ulcers began to appear, and the patient died about five weeks after first coming under observation.

Autopsy showed little of importance beyond the extensive gangrene of the entire rectogenital region. Examination for treponema pallidum, Unna-Daurey bacilli, and the Widal reaction were all negative, but blood cultures made during life showed the *Bacillus pastilis* and *spirillæ* of Vincent, and these were also found in the sanguineous secretion from the surface of the gangrenous area, occurring here in almost pure culture, with a few organisms which, on culture and animal inoculation, showed all the characteristics of diphtheria bacilli. In addition, the cultures showed the presence of a few colonies of streptococci, staphylococci, two unidentified aerobes, and colon bacilli. The other two cases of spontaneous gangrene of the female genital organs, which have been reported in the literature, were similar in practically all their manifestations—they affected young, healthy women, without albumin or sugar in the urine, pursued a rapid, progressive course, and ended fatally. No thorough bacteriologic studies were carried out in these, however.

The greater virulence of this affection in women than in men is probably due to the greater area of mucous surface subject to infection, from

<sup>1</sup> Paris Méd., 1913, vol. ix, p. 319.

which extensive absorption is possible, and in which cicatrization and healing are difficult to bring about. While the pathogenesis must be considered as practically unknown, the authors suggest that the symbiosis of several groups of pathogenic organisms may be the governing factor. Treatment can therefore be only symptomatic—an attempt to limit the area of destruction.

**Gangrene of the Cervix.** Oastler<sup>1</sup> reports a most unusual case of gangrene involving the genital region, which occurred in an unmarried girl, aged twenty-six years. Three years ago she spilled some acid on the right wrist, which left a scar about two inches square. A year after the injury small vesicles began to appear in this scar, gradually increasing in size until the skin finally sloughed away, leaving an unhealthy, necrotic, raw surface. The patient's general condition was good, and no cause could be determined for the ulceration. After about six weeks the diseased tissue was removed, and healthy skin taken from the thigh was grafted upon the area. The grafts healed readily, but the wound on the thigh very slowly, though no necrosis occurred. Microscopic examination of the diseased tissue was negative. The wrist wound remained healed for about eight weeks, then the same condition recurred, and the operation was repeated, more skin being transplanted to cover the raw surface, which this time healed permanently. Five months later the patient noticed a similar small area of necrosis over the crest of the left ilium, at a point where pressure of a corset steel had caused a slight scar; this wound healed slowly after about six months of treatment.

The girl then began to complain of a disagreeable discharge from the vagina, and of some discomfort in this region, although otherwise her health was good. Examination showed several small vesicles on the cervix, with an area of necrosis similar to those found on the skin, this area extending into the anterior vaginal fornix. The application of drying powers had apparently no effect, and the process spread over most of the cervix and anterior vaginal wall, but the resulting ulceration became finally healed, and remained so. Microscopic examination of sections from the ulcers showed merely areas of necrosis, with degenerative changes in the bloodvessels. The Wassermann reaction, blood, and urine examinations all were negative, and nothing was found to explain the condition.

A case presenting features in some respects similar to the foregoing, but in which the etiology was eventually determined, is reported by Herrgott.<sup>2</sup> The patient was aged thirty years, VII-para; was admitted to the hospital with fever and a rapid pulse, giving a history of having recently had a spontaneous abortion at about the second month. Examination showed an enlarged, edematous, and yet indurated cervix;

<sup>1</sup> American Journal of Obstetrics, 1914, vol. lix, p. 126.

<sup>2</sup> Ann. de Gyn. et d'Obst., 1914, vol. xli, p. 13.

the uterine cavity was empty. The following day the cervix appeared enormously swollen, soft, and reddish in color, with brownish-green spots, this latter discoloration extending to the vaginal vault. At first sight the appearance almost suggested a malignant tumor.

Various antiseptic douches produced no amelioration in the local condition, and the patient's general condition grew so rapidly worse that she became frightened, and after several days finally confessed that she had made three attempts to bring on an abortion by inserting a knitting needle into the uterus, following this by the injection of a *concentrated bichloride solution*. The first of these attempts had been made twelve days before admission to the hospital, the others at intervals of two days each; two hours after the last injection the patient had been seized with violent pains in the abdomen, followed by free bleeding for several days, and then by severe chills and fever, which had brought her to the hospital.

Gradually the entire cervix became gangrenous; large shreds of necrotic tissue were discharged, accompanied by an extremely fetid odor, and eventually the cervix completely sloughed away, together with the upper portion of the vaginal fornices, notwithstanding the free use of various antiseptic injections. Bacteriologic examination of the discharged shreds of tissue showed a mixed anaerobic infection.

After a brief period of apparent improvement, the patient was seized with symptoms of pulmonary embolism, and died from a condition of general pyemia. The autopsy showed complete absence of the cervix, and a cavity the size of an orange in the base of the broad ligament. In the walls of this were several large thrombosed veins containing pus, and evidently representing the point of origin for the terminal infection. The author thinks that the injections of concentrated bichloride solution were undoubtedly responsible for the onset of the gangrene, to which the fatally ending infection was of course secondary.

**Formation of an Artificial Vagina from the Sigmoid.** Among the various methods which have been recommended for constructing an artificial vagina, the most popular has heretofore undoubtedly been that of Baldwin, which consists in isolating a segment of ileum, establishing continuity of the gut by end-to-end or lateral anastomosis, and then drawing down the isolated segment in the shape of a "U" to form the new vagina. This operation is open to several objections, however, among which are, the formation of a mesenteric band with two raw surfaces, passing through the entire abdomen, and therefore giving an opportunity for adhesions, the occasional retraction of the strongly pulled-down intestinal loop, with consequent defeat of the entire purpose of the operation, or the occurrence of gangrene of the loop, resulting from interference with its blood supply. Schubert,<sup>1</sup> Albrecht, and others have, therefore, attempted

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1912, p. 249.

to use the large intestine, sigmoid flexure, or rectum, but all methods heretofore described have approached the operative field by the perineo-sacral route; such an operation is attended with great technical difficulties, both from the point of view of control of hemorrhage and of asepsis. In the use of the rectum, moreover, there is always danger of sphincteric insufficiency subsequently, so much so that several operators have formed an anus sacralis, rather than attempt to restore the intestinal continuity to the sphincter. All these operations require, moreover, more or less extensive resection of the sacrum or coccyx, which adds considerably to the seriousness of the undertaking.

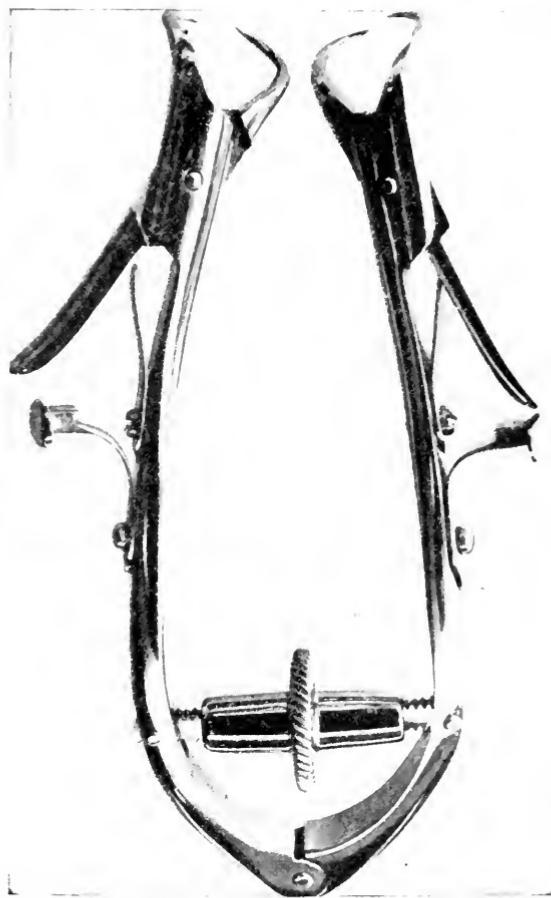


FIG. 105

Ruge<sup>1</sup> has therefore evolved an operation which combines the employment of the large intestine with the technical advantages of the

<sup>1</sup> Deut. med. Wochenschr., 1914, vol. xl, p. 120.

abdominal route, and has applied it recently with great success to a case of complete absence of the vagina and uterus. The abdomen was opened by transverse incision, the pelvic organs exposed, and a portion of the sigmoid, 15 cm. in length, which could be easily drawn down to the vulva, was resected. The two ends of this isolated segment (which of course remained attached to its somewhat mobilized mesentery) were then inverted with a purse-string suture, and the severed ends of the remaining sigmoid joined by end-to-end anastomosis. A pair of forceps were then thrust upward from the vulva, through the perineum into the pelvis,

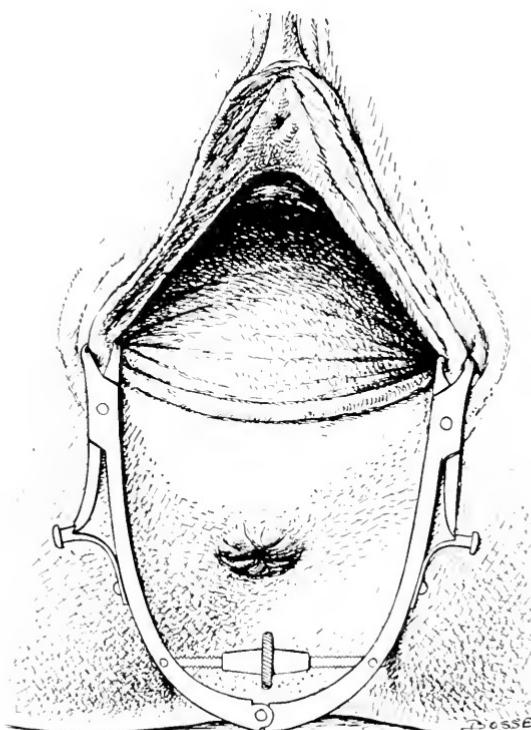


FIG. 106

and by means of them the suture attached to the lower end of the isolated segment was drawn down until it protruded about a centimeter outside the vulva. At the point where the intestine passed through the pelvic floor, the peritoneum was attached with a couple of catgut sutures to its serous surface. The inner end of the isolated segment now lay, freely movable, to the right of the rectum in the small pelvis, its pedicle crossing the sacrum to reach the sigmoid region. After attaching the remaining mesosigmoid to the pedicle of the isolated segment in such a manner as practically to shut off the latter from the remainder of the abdominal contents, the abdominal wall was closed. The ligature was

now removed from the lower end of the intestinal segment protruding from the vulva, and its mucosa united by a circular suture with that of the vulva.

Convalescence was uneventful; upon leaving the hospital the patient had a vagina 15 cm. long, easily patulous for a large finger, and non-sensitive. Examination five weeks later showed a maintenance of the same condition.

**Self-retaining Retractor for Use in Perineorrhaphy.** A useful little instrument has been devised by Friedman<sup>1</sup> to facilitate the performance of perineorrhaphy, especially when it is necessary to work with insufficient assistance. The two points corresponding to the carunculae myrtiformes, or remains of the hymen, are caught by the instrument as shown in the illustrations (Figs. 105 and 106), the arms being separated by means of the screw to the extent desired, exposing thereby the field of operation, and obtaining an equal traction on both sides. As suturing proceeds, the traction is gradually decreased by turning the screw, bringing the arms closer together. The instrument is four inches long, and the arms separate to a distance of three and a half inches, each having a firm tenaculum catch at the end.

## GONORRHEA IN THE FEMALE.

**Norris' Monograph.** One of the most important and painstaking contributions to this subject which has appeared for some time is the exhaustive monograph published during the past year by C. C. Norris.<sup>2</sup> Owing to its length, and the detail with which the author's experiences, and those of others, are recorded, it is possible in a brief review to pick out merely a few of the most salient features for consideration.

**HISTORICAL.** The book opens with a historical chapter of great interest, in which the author has traced the disease from ancient times down to the present day, showing that during antiquity and the middle ages it was known, but was largely neglected on the part of reputable physicians, who considered its treatment beneath their dignity, as a result of which it often acquired a high degree of virulence, and, in conjunction with syphilis, with which it was greatly confused, swept through the population at times as a dreadful scourge. Indeed, it was only with the fundamental work of Neisser in the later seventies that the confusion between the two diseases was entirely dissipated, and a true scientific study of the problem begun.

**BACTERIOLOGY AND PATHOLOGY.** In the succeeding chapters, the bacteriologic and pathologic aspects of the problem are discussed, under the former heading the technique of practically all the standard stain-

<sup>1</sup> Surgery, Gynecology, and Obstetrics, 1913, vol. xvii, p. 119.

<sup>2</sup> Gonorrhea in Women, Philadelphia and London, 1913.

ing and cultural methods being given in detail. The chapter on pathologic changes produced in the female generative organs is well illustrated with gross and microscopic drawings, and presents in concise form a summing up of our present knowledge of the concrete tissue alterations resulting in the female genital tract from gonorrhreal infection. Under the heading "Pathogenesis," Norris clearly emphasizes the point that, while occasionally a woman may contract gonorrhea from accidental contamination, certainly 99 per cent. of the cases occurring in adults are due solely to sexual intercourse. Although several groups of statistics indicate that in the majority of instances symptoms appear about the third day after infection, in not a few cases the disease may remain latent for a considerable period of time, owing perhaps to an original infection only of the urethra and external genitalia; in other cases, the disease becomes manifest and transmissible only around the menstrual periods. If these possibilities, and also that of a husband becoming reinfected from his wife, whom he had previously infected, are not kept in mind by physicians, totally unfounded charges of infidelity, with resulting divorce actions, may at times arise.

**SOCIOLOGY AND PROPHYLAXIS.** The enormous amount of suffering and unhappiness that have been caused in the world by this disease can scarcely be estimated, owing to the difficulty of obtaining accurate statistics, and to the fact that most cases of death really due to gonorrhœa are tabulated under other headings. Certain it is, however, that the percentage of adults of both sexes who have been at some time infected is very large, though here especially, statistics as to the number of such in proportion to the total population vary so greatly as to be of doubtful value. Prostitution is of course by far the most important source of infection for men, from whom in turn the disease is yearly transmitted to thousands of innocent wives.

The author takes a strong stand in favor of prophylactic measures, believing that this subject have in the past been treated with too much disdain, especially by English-speaking peoples. He believes in sex instruction for children of about fourteen years, and also for adults, to be carried on by responsible educational bodies in a sane and common-sense manner, avoiding particularly all obvious moral teaching and the expression of virtuous platitudes, which tend always to weaken the force of the argument.

With regard to the question which, from the sociologic point of view, assumes the position of paramount importance—prostitution—the author takes the stand that while regulation is theoretically possible, and indeed has shown excellent results in some small communities, such as army posts, on a large scale it is practically impossible to enforce such regulation with sufficient stringency to be of any service. Even were it possible to carry out with some degree of efficiency regulation of all inmates of houses of ill repute, there will always remain a large

and important class of "clandestine prostitutes"—girls, mostly of the working classes, who are immoral as a result of economic conditions—that no form of regulation can hope to reach. Moreover, an obstacle to official regulation will always be presented, in this country at least, by the strong public sentiment against it. From a consideration of these and various other arguments, pro and con, the author has come to the conclusion that regulation is at best of comparatively minor importance in the question of the prophylaxis of venereal disease, compared with educational and other measures, which appear to offer a far better prospect for the ultimate solution of the problem.

One of the most important of these measures Norris considers to be a change in the attitude of the hospitals in this country, a vast majority of which have no adequate accommodation for venereal patients, and most of which in fact refuse to admit them at all. It is self-evident that the most efficient regulation of female prostitutes would be of little ultimate avail, if provision is not made for sterilization of the source of infection by prompt and thorough treatment of all male gonorrhoeics. The establishment by municipalities of facilities for free bacteriologic and serum tests, placing venereal disease on the reportable list, improved instruction in the diagnosis and treatment of this group of diseases in our medical schools, and the passage of laws requiring a certificate of health from the man before marriage, are among other methods recommended for lessening the prevalence of gonorrhea. The remarkable results obtained in the military and naval services of this and other countries by the use of certain antiseptic preparations for the purposes of personal prophylaxis are discussed at length, with the details of the various procedures employed.

In short, the author considers that the two important points to be emphasized in our attitude toward venereal disease, from the point of view of the community, are the cure of the diseased, and the protection of the uninfected; in attaining these objects we should not be hampered by moral doubts and platitudes, but should utilize every weapon at our command.

**THERAPY.** After a systematic discussion of the therapeutic procedures commonly employed in the local treatment of gonorrhreal infection of the various portions of the female genital tract, the author takes up the consideration of the surgical treatment of the end-results of such infection—the group of lesions commonly included under the term "pelvic inflammatory disease." Basing his judgment largely on the results obtained in the past decade at the Gynecological Clinic of the University of Pennsylvania, he draws his conclusions strongly in favor of the conservative type of procedure—*i. e.*, subjecting practically all patients with pelvic inflammatory disease to a course of preliminary treatment before operation is undertaken, and then observing a rational conservatism with regard to what organs shall be removed. Norris

favors waiting, if possible, until the patient's temperature and blood counts have been normal for as much as from four to six weeks before operating, since if this be done, some will escape operation altogether, while in others more conservative procedures will be possible than had operation been attempted in a more acute stage. Conservation of a grossly normal tube in the presence of diseased appendages on the opposite side is advocated; macroscopically diseased tubes should be removed, however, as attempts at their conservation, with or without the performance of salpingostomy, are usually unsatisfactory. In the author's experience, pregnancy has rarely occurred after such operations, the newly formed ostia quickly closing and causing a recurrence of the symptoms. Conservative ovarian surgery—even resection, with retention of only a small amount of ovarian tissue—is advocated in suitable cases, the important point to be observed being the maintenance of a satisfactory blood supply to the conserved ovarian tissue. Even if the uterus has to be removed, one or both ovaries should be spared if possible, as this unquestionably tends to prevent the distressing nervous symptoms associated with an artificial menopause. When both ovaries have to be removed, however, Norris advocates performing a hysterectomy in most cases, since uteri left behind under these conditions are useless, and often give rise to subsequent trouble, but he does not advocate removing the entire uterus, supravaginal amputation being a simpler and quicker operation, which gives quite as satisfactory results as panhysterectomy, providing the cervix is well cupped out, and the mucosa entirely destroyed by the actual cautery. The latter point he considers very important, most of the reported cases of subsequent trouble being due to faulty technique in this particular.

The question of cancer subsequently occurring in the cervical stump is perhaps worthy of consideration, but must be of such rare occurrence as to be almost a negligible factor; the author reports having seen but one instance of a cervical carcinoma developing after supravaginal hysterectomy. Drainage should be employed only in the exceptional case—where, for instance, it has been impossible to remove the entire abscess-sac, where it has been necessary to leave behind a large amount of lymph, or where some abdominal viscera has been considerably injured. When drainage must be employed, the vaginal route is to be preferred to the abdominal under ordinary circumstances.

**GONORRHEA AND PREGNANCY.** Although, of course, gonorrhea is in numberless instances the cause of female sterility, it by no means invariably prevents conception. A pregnancy, occurring in a gonorrhoeic, may be interrupted as a result of the pelvic lesions which the disease has caused, or may proceed to term. In the latter case, the influence of the pregnancy on the course of the gonorrhea is of considerable importance, the increased blood supply of all pelvic organs incident to gestation rendering them unusually susceptible to infection, and aggravating

the resulting pathology. Various observers have estimated the proportion of gonorrhœas among pregnant women at from 5 to 30 per cent., the more conservative figures probably being more nearly correct, however. That the gonococcus plays an important part in the production of puerperal infection has also been conclusively demonstrated.

In the presence of a suspected or demonstrated gonorrhœa in a pregnant woman, a daily douche of 1 to 5000 bichloride during the last week of pregnancy, and an antepartum vaginal douche of lysol or some other antiseptic, are strongly recommended, more as prophylactic measures from the point of view of the child than with any idea of curing the disease. An additional safeguard is furnished by painting the external genitalia with iodin as soon as labor commences. In the treatment of puerperal infection of gonorrhœal origin, any retained secundines should be removed manually, but under no circumstances should the uterus be curetted. Beyond this, symptomatic and expectant treatment is to be employed, no operation being undertaken in the acute stage, except when it is possible to evacuate pus without opening the peritoneal cavity, or when a diffuse peritonitis develops.

**SEROTHERAPY.** The concluding chapters deal *in extenso* with the more unusual complications of gonorrhœa, and with its various extragenital manifestations; in a final word upon vaccine and serum therapy, the author comes to the conclusion that markedly beneficial results have undoubtedly been obtained by these forms of treatment in certain classes of cases—especially arthritis, and in vulvovaginitis of children, but that much extensive experimentation is still necessary to put the use of sera and vaccines upon a firm scientific basis.

**Complement-fixation Test for Gonorrhœa.** Considerable attention has been paid during the past year to the complement-fixation test for the diagnosis of gonorrhœa, the general principles of this being similar to those of the Wassermann test for syphilis. Owen and Smire<sup>1</sup> have performed the test on a series of 100 patients presenting various clinical conditions, and are convinced of its reliability, providing it is done with polyvalent antigens, as advised by Schwartz and McNeil.<sup>2</sup> Except in the very acute stage (during the first three weeks), they have found the reaction practically uniformly positive where gonococci were demonstrable under the microscope; its greatest value, however, is in the detection of chronic cases harboring a focus of infection, but in which no gonococci can be found microscopically.

The authors have never obtained a *positive* reaction in a patient in whom the existence of a previous gonorrhœa could not be demonstrated, or at least strongly suspected; *negative* reactions are not so conclusive, however. They believe the test will be of great service in those states which require a certificate of health before marriage, as its performance

<sup>1</sup> Journal Michigan State Medical Society, 1913, vol. xii, p. 247.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1913, p. 254.

is accompanied by none of the exposure attendant upon physical examination, and the results are far more accurate, except in the acute stages of the disease.

Rockwood<sup>1</sup> has performed the test on 158 patients with similar results. He has never obtained a positive reaction in a case in which the absence of gonorrhreal infection was certain, but in 2 cases which gave a negative reaction, a urethral discharge was present containing Gram-negative diplococci. The reaction was positive in over 80 per cent. of cases in which the possibility of an active gonorrhreal infection was indicated either by bacteriologic findings or from the history; in over 80 per cent. of *clinically cured* cases, a *negative* reaction was obtained, and in no such case has there been any evidence of a recurrence of the disease. While the gonorrhea complement-fixation test furnishes probably no exception to the rule that all clinical tests are subject to a certain amount of error, the results appear sufficiently constant to give the test a great value from a clinical standpoint.

In both the above series of investigations, the polyvalent gonorrhreal antigen, prepared by Parke, Davis & Company from ten or more strains, was used.

Lespinasse and Wolff,<sup>2</sup> on the other hand, have made their own antigens from cultures of various strains of gonococci. In 25 cases absolutely free from gonorrhreal history the test was universally negative. Of 12 clinically cured cases of one year's standing, 3 were positive and 9 were negative; of 9 clinically cured cases of two years' standing, 1 was positive and 8 were negative; of 47 such cases of from three to ten years' standing, all were negative.

Treatment of an individual by gonorrhreal vaccines will render the complement-fixation test positive, whether he has had gonorrhea or not, so that it cannot be relied upon in patients who are being treated in this manner. Since the test will detect the presence of the gonococcus anywhere in the body, and in any variety of the disease (after the fourth week), however, it is of great value in clearing up obscure lesions of uncertain etiology, such as arthritic conditions, iritis, etc. In gynecologic work, the authors think it may be of great assistance in showing whether a leucorrhea is gonorrhreal or non-gonorrhreal in origin, whether a pus tube is of gonorrhreal or other etiology, whether a pelvic cellulitis or peritonitis is due to gonorrhea, in differentiating an acute appendicitis from an acute pus-tube, in explaining the occurrence of puerperal fever in apparently cleanly handled cases, and in detecting cases antepartum in which very special attention should be given to the baby's eyes.

Thomas and Ivy<sup>3</sup> have also tried out the gonococcus complement-fixation test in about 200 cases, using for the most part a hexavalent

<sup>1</sup> Cleveland Medical Journal, 1913, vol. xii, p. 1.

<sup>2</sup> Illinois Medical Journal, 1913, vol. xxiii, p. 26.

<sup>3</sup> Arch. Int. Med., 1914, vol. xiii, p. 143.

antigen which they prepared themselves from six stains of gonococci furnished by the Mulford Company. This proved much more constant in results than monovalent and trivalent antigens, which they tried for comparison. The conclusions at which they have arrived correspond quite closely to those of the other authors already quoted; they are convinced that a positive reaction is invariably reliable, and always denotes the presence somewhere of a gonococcal infection, since in no alien condition have they ever obtained a positive result. They agree, therefore, with Schwartz and McNeil in considering the gonococcus fixation test distinctly more specific than the Wassermann. In about 20 per cent. of clinically cured cases they have found a persistence of the reaction; no such patient should, in their opinion, be discharged from treatment or observation until a negative reaction is obtained, unless he has been receiving gonococcal vaccines, which may be responsible for the formation of antibodies in the blood.

Although most of their work has been done on males, Thomas and Ivy believe that the test is destined to play an important role in the differential diagnosis of pelvic disease in women. They have tried it in a few gynecologic cases, but have not been able to obtain positive results in uncomplicated urethritis, vulvovaginitis, and Bartholinitis, and conclude, therefore, that the infection must ascend at least to the level of the uterus in order to produce a positive blood reaction.

They bring out an interesting point from the stand-point of forensic medicine, namely, that during the acute stage of the disease, while the fixation test is almost invariably negative, it is, as a rule, comparatively easy to demonstrate the presence of gonococci bacteriologically, whereas in the chronic stage, when bacteriologic methods frequently fail utterly, the fixation test becomes positive and clears up the situation, the two methods of examination being, therefore, in a sense complementary to each other.

**Local Treatment of Acute Gonorrhea.** Slingenberg<sup>1</sup> thinks that gonorrhreal affections of the urethra, vulva, vagina, and uterus are among the most wofully neglected of all diseases. Many men make no attempt to treat acute gonorrhreal infection in women, believing on the one hand that such treatment is absolutely without benefit, and on the other hand that the gonocoeci will eventually disappear without treatment. He emphasizes the incorrectness of both of these opinions, and says that after much experimenting he has finally adopted the following technique, which has given him most gratifying results in the treatment of this particularly stubborn class of cases:

The urethra is irrigated once daily with a *freshly prepared* 10 per cent. protargol solution, made by placing one gram of powder in 10 c.c. of cold water three hours before the treatment is to be given, keeping the

<sup>1</sup> Zenttbl. f. Gyn., 1913, vol. xxxvii, p. 1450.

bottle in the dark. The injection is made with a syringe covered by a bulbous-tipped catheter, the bulb being large enough to flatten out the urethral mucosa. It is inserted until resistance of the sphincter is felt, and then as the syringe is slowly emptied, the catheter is drawn back and forth a couple of times throughout the entire length of the urethra. By means of a speculum, the cannula of a Braun's syringe, filled with the same fluid, is then introduced to the fundus of the uterus, the syringe being gradually emptied as the cannula is withdrawn. The remainder of the fluid is poured into the speculum, and just sufficient gauze is then introduced into the vagina to absorb it. Finally, a small strip of gauze is placed between the labia, to be renewed after each urination. In addition to this local treatment, vaccine therapy is applied. The patient must be kept in bed, and receives two capsules of 0.3 gram "gonosan" t. i. d.

If after a week or so the vaginal, cervical, and urethral secretion is free from gonococci, the protargol solution is replaced by a solution of zinc sulphate and lead acetate — 1 gram, to 100 c.c. of water for the urethra, and a mixture of boric acid 3 grams, aluminol 5 grams, camphor 3 grams, glycerin 125 c.c. for the vagina. When the secretion remains free of gonococci, even after vaccine injections running up to 100,000,000 organisms at a dose, the case is considered cured. The local treatment usually lasts from three to six weeks.

Hofmann<sup>1</sup> strongly recommends the iodine treatment originally proposed by Bovée, and says that he has had most excellent results with the following technique: As soon as establishing a diagnosis, he paints the labia, urethral orifice, Skene's ducts, and the entire vagina and vaginal surface of the cervix with tincture of iodine. If the infection has penetrated to the interior of the uterus, the cervix is treated by an applicator, and some of the iodine solution is injected into the uterine cavity by means of a syringe, which is introduced till the tip reaches the fundus, the fluid being slowly forced out as the syringe is withdrawn. This treatment is repeated every third day for three sittings — a couple of days later, careful search for gonococci should be made; if none are found, the author considers that the treatment may be discontinued; if organisms are still present, however, it is to be continued longer in conjunction with vaccine therapy.

## SYPHILIS.

**Syphilitic Changes in the Uterus.** Chase<sup>2</sup> calls attention to the remarkable lack of attention given to syphilitic changes by gynecologists. The majority of text-books on surgery and gynecology either do not

<sup>1</sup> Interstate Medical Journal, 1913, vol. xx, p. 733.

<sup>2</sup> Texas State Journal of Medicine, 1913, vol. ix, p. 95.

mention syphilitic changes in the female genital organs, or pass them over in a few lines; moreover, careful search through the exhaustive index of the world's medical literature, published by the American Medical Association, failed to produce a single reference to any article on this subject during the last four years. From this it must not be assumed that syphilis of the organs specially interesting to the gynecologist does not occur, however, for sufficiently well-established cases have been reported in the literature from time to time to show the existence and importance of such lesions.

*Chancres of the Cervix* is the commonest form of uterine syphilis, or at least has been the one most frequently recorded. In the author's experience, chancres in this situation are more similar in appearance to mouth infections than to the usual penile manifestations; they may appear as yellow, apparently fat-covered ulcers, or as shiny, indurated plaque-like syphilides, such as occur in the tongue and soft palate. They are often obscured by lacerations or mucus, and hence escape detection, or are mistaken for Nabothian cysts. When the cervix is the seat of more massive infiltration, a condition is produced which may easily be mistaken for malignancy.

In the author's opinion, however, *syphilitic endometritis* is in reality the commonest form of uterine syphilis. In a few instances, distinct gummatous formations have been found, in others merely a hypertrophic fungoid endometritis, with areas of cicatrization and periarteritis. The chief symptoms are usually profuse leucorrhæal discharge or metrorrhagia; they clear up rapidly under antisyphilitic treatment, but remain unaffected by all other forms of therapy.

Definite studies of syphilitic conditions of the adnexa are even more scanty than of the uterus, but Chase believes that if proper attention were directed to the subject by gynecologists, using the modern methods of diagnosis at our command, a practically new chapter of gynecologic pathology would be opened up, and it would be found that syphilis of the adnexa is by no means so uncommon as is generally supposed.

**The Wassermann Reaction in Gynecology.** McIlroy and Watson<sup>1</sup> report a series of 100 Wassermann tests made on patients from the Royal Infirmary, Glasgow, who were suffering with various gynecologic disorders. None of these women presented obvious symptoms of syphilis, yet 43 gave positive and 9 doubtful reactions. So large a proportion is very surprising, and would certainly, the authors admit, arouse a suspicion as to the technique, but a control series upon 69 healthy children, carried out in exactly the same way, were all negative. Especially in cases of metrorrhagia, without tumor or other demonstrable cause, is a syphilitic etiology to be considered, and in many of the cases in the series reported marked improvement occurred under antiluetic

<sup>1</sup> British Medical Journal, 1913, No. 2755, p. 1002.

treatment. The authors suggest the importance of a more careful investigation by gynecologists into the possibility of a latent and unsuspected syphilitic factor in many of their cases.

### THE FEMALE URINARY SYSTEM.

**Anomalous Renal Vessels.** Ruppert<sup>1</sup> calls attention to the much greater frequency of an anomalous arrangement of the renal vessels than is generally recognized, and of the surgical importance of the realization of this fact. He has carefully studied the vascular relations of both kidneys from 50 cadavers used for routine dissection at the University of Illinois in 1912-1913. In all of these, both organs were normally placed, there being among them no movable, pelvic, or horseshoe kidneys, nor had any been removed at operation. He found some anomalous arrangement of the arteries on the left side in 13 cases; on the right side in 11; and on both sides in 10. Of the veins, there were anomalies on the left side in 2; on the right side in 9; and on both sides in 2. Anomalies of both veins and arteries in the same specimen occurred on the left side in 1; on the right side in 3; and on both sides in 1.

Although anomalous veins are not as frequent as anomalous arteries, they are of equal importance when they do occur, as their presence may increase the hazards of renal operations, especially nephrectomy. Because of the thinness of their walls, they give but little if any more resistance to traction than would a small adhesion, and as pulsation is absent, such an anomalous vein is difficult to differentiate from an adhesion, unless it can be drawn definitely into the field of vision.

**Abnormal Vessels as a Factor in Hydronephrosis.** A Scandinavian surgeon, Borelius,<sup>2</sup> reports in detail 5 cases of nephrectomy on account of hydronephrosis, all occurring in women, and in all of which the presence of an abnormal vessel going to the lower pole of the kidney, and therefore crossing the ureter, was a factor in the causation of the condition. In all the specimens, moreover, the relations were such as to confirm the principle formerly enunciated by Ekehorn<sup>3</sup> that vessels which pass *in front* of the ureter to the *anterior* edge of the kidney hilus, or those which pass *behind* the ureter to the *posterior* edge of the kidney hilus do not compress the ureter at all, and therefore have no effect in the production of hydronephrosis. A vessel, however, which passes *in front* of the ureter to the *posterior* edge of the hilus, or *vice versa*, can cause distinct constriction of the ureter as the renal pelvis fills, the latter tending to lie on one side of the vessel, and the former on the other.

<sup>1</sup> Surgery, Gynecology, and Obstetrics, 1913, vol. xvii, p. 580.

<sup>2</sup> Folia urol., 1913, vol. vii, p. 621.

<sup>3</sup> Arch. f. klin. Chir., vol. lxxxii, p. 44; Fol. urol., vol. i, p. 755; vol. ii, p. 96.

It seems hardly conceivable, however, that the mere presence of the vessel anomaly alone, without some other factor to cause overfilling of the renal pelvis, should in many instances give rise to a true hydronephrosis, for even in the presence of such a vessel, the ureter would in most instances be easily deflected sufficiently to prevent obstruction; that this is true is shown by the fact that although the anomalous vessel in all cases is congenital, the symptoms of hydronephrosis usually develop only in adult life. Such an additional factor might easily be furnished, the author thinks, by a slight degree of excessive mobility of the kidney, or by pressure from a gravid uterus, abdominal tumors, or inflammatory processes, which might cause a temporary obstruction to the urinary flow and distention of the renal pelvis, thus predisposing the kidney to permanent hydronephrosis when in addition there is present a real hinderance, such as an abnormal vessel.

In all 5 cases reported by Borelius, the history and operative findings indicate with more or less clearness that an abnormal mobility of the kidney was the predisposing, and the anomalous vessel the determining cause of the hydronephrosis. He advocates, therefore, early operation in all cases of hydronephrosis, as in this way the kidney may often be saved by doubly ligating and cutting the anomalous vessel, or if this appears of great importance for the nourishment of a considerable portion of the kidney, he goes so far as to suggest cutting the ureter at the point of crossing, and implanting the lower segment in the renal pelvis on the other side of the artery. He apparently has not himself carried out this rather remarkable suggestion, however. If the kidney is out of place, it should of course be suspended.

**Origin of Congenital Cystic Kidneys.** The pathogenesis of the congenital cystic kidney has never as yet been definitely determined, and there exist still considerable differences of opinion among pathologists and embryologists upon this subject. For the most part, however, the older inflammatory and neoplastic theories have been given up, and have been replaced by the belief that these cases arise from a failure of union between the secreting and excreting portions of the renal mechanism, it having been shown pretty conclusively that these two systems arise primarily from totally different embryologic structures, which secondarily should fuse and form one continuous system of conduits from the glomeruli to the renal pelvis. In an attempt to clear up some of the obscure points in connection with this theory, a careful study of a congenital cystic kidney from a slightly premature fetus has been made by Forssman<sup>1</sup> by means of the plastic reconstruction method commonly used in embryologic work. As there was very little evidence of inflammation present, Forssman considered this specimen specially suited for the study of the origin of the cysts.

<sup>1</sup> Beitr. z. Path., Anat. u. z. allg. Path., 1913, vol. lvi, p. 500.

He found that interruptions in the continuity of the uriniferous tubules could occur at practically all levels of the kidney, from the straight collecting tubules to the glomeruli, and that cyst-formation could also occur in all possible portions of the kidney, from the pelvis to the cortex, the position of a given cyst not necessarily having any direct relation to the point at which its excretory canal had become occluded, but rather to the *consistency of the surrounding interstitial tissue*. Wherever this latter is specially loose and open, cystic dilatation of the canal system can most easily occur.

Forssman believes that the origin of these cysts is due, not so much to a primary failure of the collecting portion of the tubules, coming from the ureteral anlage, to unite with the convoluted tubules, coming from the true renal anlage, as to a *secondary obliteration* of the collecting tubules *after* such union has originally taken place, but the *cause* of this obliteration he was entirely unable to determine. It seems probable that such tubules collapse below the point of obliteration, and undergo complete disappearance.

**Histologic Diagnosis of Vesical and Renal Tuberculosis.** Buerger<sup>1</sup> describes a new method of diagnosis which stood him in good stead in a case of early renal tuberculosis without definite symptoms. The patient complained of pain in the lower abdomen, and great frequency of urination. The urine was clear, no tubercle bacilli could be found, and cystoscopic examination was negative, except for a slight edema around the left ureteral orifice and in the left half of the trigone, but without any sign of tubercles or ulceration. On account of the edema, a sound could not be passed into the left ureter, but the right side was easily catheterized, and clear urine obtained. A tentative diagnosis of tuberculosis of the left kidney was made, but to confirm this, a few small bits of the edematous mucous membrane about the left ureteral orifice were excised by means of the author's operating cystoscope and special forceps; histologic examination of these pieces of tissue showed marked edema and several distinct miliary tubercles, most of which were distinctly beneath the surface, explaining their absence from the cystoscopic picture. A positive diagnosis of tuberculosis was therefore made, and was confirmed by the subsequent nephrectomy, a kidney being removed which showed very early tuberculous lesions—numerous miliary tubercles, with here and there just beginning areas of caseation. The renal pelvis and ureter were almost entirely free.

The author thinks that in doubtful cases, such as the foregoing, this method may be of great value in establishing an early diagnosis.

**Idiopathic Hematuria.** A condition which often proves exceedingly puzzling both to the pathologist and clinician is that of so-called "essential hematuria," usually unilateral, and occurring without any demon-

<sup>1</sup> Jour. d'Urol., 1913, vol. iii, p. 1.

strable cause, such as renal tumor or stone. A considerable number of such cases have been reported in the literature, and various methods of dealing with them have been suggested. While most surgeons favor conservative measures, such as decapsulation or nephrotomy, which in the large majority of instances appear to be entirely effectual in checking the hemorrhage, a few men advise and practise nephrectomy, arguing that the condition is almost always unilateral, that a kidney which is the seat of any considerable amount of hemorrhage must have undergone profound pathologic changes, even if these cannot be definitely demonstrated, and that the opposite organ is quite sufficient to carry on the work of elimination. That in some instances, however, the assumption of the unilateralness of the underlying lesion is utterly fallacious, even in the presence of purely *unilateral symptoms*, and that therefore radicalism is a dangerous doctrine to teach in regard to these cases, is well shown by a case reported by Kretschmer<sup>1</sup> of right unilateral hematuria, which disappeared after decapsulation of the right kidney. Three and one-half years later, the same condition developed on the left side, and was relieved by a similar operation on the left kidney. There were no albumin or casts in the urine at any time, but pieces excised from each kidney showed distinct nephritic changes. An extensive study of the literature has shown that in practically all these cases a mild grade nephritis is an etiologic factor, and that, as in this case, a *unilateral renal hematuria* may exist with a *bilateral lesion*.

Payne and Macnider<sup>2</sup> have tried three series of experiments on dogs, in the attempt to discover if possible some definite etiologic factor in the production of these "essential" unilateral hematuria cases.

In the first series of experiments, the vasoconstrictor nerves were cut. These reach the kidney in two groups one running along the renal arteries, the other, less important, entering the upper pole of the kidney from the suprarenal body. By careful dissection, the authors were able to sever all structures going into the kidney except the renal artery and vein and the ureter, thus cutting off all vasoconstrictor influence. The result was the production of an acute congestion of the kidney.

In the second series, a nephrotoxic substance—sodium arsenate—was injected into the left renal artery; the urine was carefully examined, the animals then killed, and the kidneys studied histologically. They showed an acute dilatation of the glomerular vessels, with but slight involvement of the epithelium.

In the third series, the renal artery was wholly or partially compressed with a Stewart's clamp, so as to interfere with the blood supply; the animals were killed on the fourth day. The kidneys showed cloudy swelling of the epithelium, and occasional zones of coagulation necrosis. In none of the experiments was hematuria produced, and it would seem

<sup>1</sup> Surgery, Gynecology, and Obstetrics, 1913, vol. xvi, p. 34.

<sup>2</sup> Ibid., vol. xvii, p. 93.

therefore, that "idiopathic hematuria" is not due to an excessive amount of arterial blood reaching the kidney, to an acutely developing vascular injury, nor to a decreased flow of arterial blood, with consequent lowering of the arterial pressure and induction of passive congestion.

Since in all cases of idiopathic hemorrhage, occurring clinically, a *chronic inflammation of the kidney* is found, the authors believe the condition to be due to a type of nephritis in which a rupture of a glomerular vessel occurs, the bleeding thus instigated being kept up by the high local pressure found in this disease. The fact that simple nephrotomy with suture practically always cures these cases is probably explained by the relief of congestion which it brings about, together with the dissolution of the continuity of the bloodvessels, this in some way interfering with the afflux of blood. Owing to a compensatory hypertrophy of the intact parts of the kidney, which apparently occurs after this operation, the functional capacity does not seem to be diminished.

**Origin and Treatment of Pyelitis.** Oppenheimer<sup>1</sup> has reviewed the points of interest in a series of 100 cases of pyelitis from his private practice and the Frankfurt Gynecological Clinic. He agrees with those authors who consider *colon bacillus infection* the most frequent cause of this condition, although numerous other bacilli and cocci are found at times as the etiologic factor. In two of Oppenheimer's cases an organism was found—once in pure culture—which has not previously been described as the cause of pyelitis, the *bacterium fecalimum alcalinges*.

There are two modes by which bacteria may reach the kidney pelvis: either by the *ascending* route from the bladder (ureteropyelitis), or by first invading the renal pelvis, being then carried out through the ureter—the *descending* type of infection (pyelo-ureteritis). Oppenheimer considers the ascending type much the more frequent, and believes that the organisms ascend through the ureteral lumen, rather than by the lymph channels in the periureteral tissue. For this to take place, however, two conditions must be present, a relaxation of the normal valve-like action of the ureteral orifices, and a diminution of the force of the urinary stream—in other words, there must be a ureteral stasis, which may arise from various causes, such as stones, stricture, pregnancy, uterine malpositions, spinal-cord lesions, etc.

With regard to the descending type of infection, Oppenheimer thinks that in rare instances this may occur by direct continuity, or by lymphatic invasion, somewhat oftener by hematogenic infection; this latter form is to be assumed in cases where the original source of infection is at a considerable distance from the urinary system, and the lower portion of this is free from any obstruction which could account for an ascending infection.

<sup>1</sup> Zeitschr. f. urol. Chir., 1913, vol. i, p. 17.

In the treatment of the condition, Oppenheimer takes the very positive stand-point that every acute pyelitis is to be treated conservatively, *i. e.*, by rest in bed, and the administration of urinary antiseptics and large quantities of fluid. The quite general practice of giving alkaline waters is not to be recommended, unless the urine is strongly acid, since it has been shown that alkalinity of the urine favors the growth of certain bacteria. The diet should be limited to milk and gruel for the first week, then vegetables may be added gradually, but no meats or rich foods for another week or ten days; the patients should not be allowed to get out of bed until fever has been absent for ten days. The drug most favored by Oppenheimer is salol in large doses—4 to 5 grams (60 to 75 gr.) daily—sufficient to cause a distinct greenish color in the urine. These doses were well borne in all his cases except one, a frail, delicate woman, who showed some symptoms of salicylic acid poisoning. If urotropin is used, it should be given in similar doses; Oppenheimer prefers, as a rule, however, to reserve it for after-treatment, giving it then in smaller doses, and continuing it for several weeks or even months.

Although local treatment, such as ureteral catheterization, is practically never indicated in the acute stage, there are a certain number of cases which do not clear up under the general treatment outlined above, but pass over into a subacute or chronic condition, and then require more energetic measures. Oppenheimer is not a great believer in washing out the renal pelvis through the ureteral catheter; in the few cases in which he did consider this necessary, he used about 8 to 12 c.c. of a 0.5 to 1 per cent. solution of silver nitrate, introducing it under very slight pressure, and permitting it to run out again immediately through the catheter. On the other hand, he is a strong believer in *permanent drainage* for all cases which do not clear up under general treatment. This he accomplishes by introducing a large ureteral catheter into the pelvis of the kidney, and leaving it there. In cases of ordinary pyelitis of pregnancy, he leaves the ureteral catheter in place for two weeks at first; if after its removal the patient remains afebrile, conservative treatment is continued, but if the temperature again rises, the catheter is replaced for another two weeks. He says that he has not encountered any discomfort or disagreeable sequelæ from this form of treatment.

**Pyelotomy Versus Nephrotomy.** According to Eisendrath<sup>1</sup> the operation of *pyelotomy* has not received in this country the attention that it deserves, in view of the excellent results reported from the French and German clinics, many of our surgeons still clinging to the older operation of nephrotomy in all cases of nephrolithiasis, no matter what the size or situation of the stones to be removed. Eisendrath, however, believes pyelotomy to be decidedly the method of choice, in suitable cases,

<sup>1</sup> Journal of the American Medical Association, 1913, vol. lx, p. 1145.

for the removal of renal calculi. Owing to the intimate relation of numerous arterial and venous trunks to the anterior aspect of the renal pelvis, approach from this direction is impracticable, but the single retropelvic artery is quite constant, and is well within the hilum, so far away from the region in which the incision is usually made as to be practically a negligible factor, provided the incision is not carried too near to the parenchyma of the kidney.



FIG. 107

*Technique.* To perform pyelotomy, it is necessary to be able to lay the kidney completely on its anterior surface on the edge of the parietal incision, or at least to gain access to the posterior aspect of the renal pelvis without too much tension on the vessels. If the pedicle is short, or if there is much fixation by adhesions, pyelotomy is out of the question. The author's method is to introduce a fine traction suture through the wall of the renal pelvis on each side of the proposed incision; the wall is then incised, and the opening enlarged upward and downward with fine scissors (Fig. 107). The edges of the incision are now held apart by the traction sutures, and by means of a finger inserted through the incision, the entire interior of the pelvis may be easily palpated. The fingers of the other hand can at the same time palpate the outer surface of the kidney, in this way the calices and papillæ being easily felt, and any calculi present located. When these have been removed, the incision is closed with a fine catgut suture, care being taken not to pass this through the mucosa; a small cigarette drain is then inserted down to the line of incision. If the urine contains considerable pus, however, a soft-rubber drain should be sutured into the pyelotomy incision, and brought out through the posterior end of the abdominal wound.

The author considers pyelotomy superior to nephrotomy in practically all cases, except where there is a large branched calculus filling the renal pelvis, or where there are many small calculi lying scattered throughout the kidney in closed cavities. In such cases, nephrotomy is preferable, as it is also in infected cases with more or less destruction of the parenchyma, since effective drainage may be carried out far better through a nephrotomy incision than through that of a pyelotomy. The contra-indication to the latter operation in cases of extensive perinephric adhesions has been referred to above. The advantages of pyelotomy are its simplicity, the rapidity with which it can be done, and the slight amount of hemorrhage with which it is usually accompanied. Eisendrath reports one case, however, in which a nephrectomy had to be performed, owing to severe venous hemorrhage which followed the removal, by means of pyelotomy, of a calculus which was firmly held in one of the calices.

**Pyelography.** Strassmann<sup>1</sup> has studied, in 6 rabbits, the effect of injecting into the renal pelvis, under moderate pressure, a quantity of collargol considerably greater than the normal capacity of the pelvis. This was done by opening the bladder, and introducing a fine cannula or catheter into the ureter by direct vision. After making the injection a stopper was inserted into the cannula for a few minutes, and the fluid then allowed to escape. The kidneys were removed in some instances immediately, in others, after one hour, and in one experiment after twenty-four hours. Although the experiments were too few in number to permit of any final conclusions, they all accorded as far as they went. The collargol never appeared to have gotten into the collecting tubules, but some was taken up by the *lymph spaces* surrounding the tubules, and was carried to the renal capsule with the lymphatic current. By the end of twenty-four hours, the greater part of the silver had left the kidney tissue, but numerous masses were still found in the pelvis. The mucosa of the pelvis and of the tubules remained in every instance intact, the entrance of the silver salt into the lymph spaces being accomplished without any demonstrable alteration in the superficial epithelium.

From these experiments, the author concludes that when carefully carried out, the injection of collargol into the renal pelvis in the human subject is entirely without danger of injury to the kidney.

Kelly and Lewis<sup>2</sup> suggest the use of an *emulsion of silver iodide* instead of collargol in pyelography. Their objections to the latter drug are that it is dirty, staining everything with which it comes in contact, is quite expensive, and is a proprietary preparation, whose exact composition is unknown. In casting about for a substitute therefore, Kelly and Lewis hit upon silver iodide, a substance which has been used therapeutically in the bladder and urethra for some time. They find that a

<sup>1</sup> Ztschr. f. urol. Chir., 1913, vol. i, p. 126.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, 1913, vol. xvi, p. 707.

well-made emulsion will maintain the salt in suspension for a considerable length of time; it is bland and non-irritant, possesses antiseptic properties, and costs less than one-fifth as much as collargol. They believe that the fear of leaving particles of silver salt in the pelvis or ureter, to form a nidus for subsequent calculi, is entirely unfounded. For ordinary work, the authors have found a 5 per cent. emulsion strong enough, giving a shadow fully as dense as that from a 10 per cent. collargol solution, and where large cavities are to be filled, a solution as low as 1 per cent. will give excellent results.

**Diagnosis and Treatment of Ureteral Calculus.** In a comprehensive article, Israel,<sup>1</sup> of Berlin, discusses his present stand-point with regard to *ureteral lithiasis*, a subject upon which he is well qualified to speak, his personal experience covering over 60 operations, or more than one-third as many as have been reported by all other surgeons together. He thinks the explanation of the fact that so few operations are performed for stone in the ureter, as compared with those for nephrolithiasis, is to be found in *poor diagnosis*; if every case presenting symptoms at all suggestive of stone were subjected to an x-ray examination of *both kidneys and ureters*, many cases of ureterolithiasis would be discovered which are now treated for appendicitis, adnexal conditions, and cancer. In almost all instances, ureteral calculi have originated in the kidney, and have passed downward; they often, however, increase in size in the ureter by the deposition of salts, and at times reach very large proportions. In very rare instances, however, it is possible for stone to be formed in the ureter itself.

In by far the greater number of Israel's cases, the stone was lodged in the portion of the ureter in the small pelvis (64 per cent.); in 21 per cent. it was in the lumbar portion (above the crest of the ilium); in 11 per cent. in the iliac portion (between the crest of the ilium and the brim of the small pelvis); in only 4 per cent. in the intraparietal portion, *i. e.*, that part which traverses the bladder wall. In women, quite a large proportion of the intrapelvic stones are palpable through the vagina, and in a few instances very large stones may even be felt through the abdominal wall. Occasionally a spastic contraction of the ureter which may simulate stone will occur on palpation, but if the finger be kept quietly upon the spot for a few minutes, the contraction relaxes, and the supposed stone disappears. This must not be confused with the slipping upward, beyond the palpating finger, of a real stone, which may easily occur when the ureter is dilated. A stone may also be displaced by the ureteral catheter, or the catheter may slip past a stone and enter the renal pelvis, apparently without obstruction; even a metallic, non-elastic sound may slip by a small, deeply embedded concretion, and give no indication of its presence.

<sup>1</sup> Folia Urologica, 1913, vol. vii, p. 1.

While the *symptoms* may be strongly suggestive, they are rarely absolutely diagnostic, so that *actual palpation* and *skiagraphy* must always remain our most important diagnostic methods. In employing the latter, the use of a shadowgraph-catheter is of course of the greatest importance, and at times cases occur in which a stereoscopic skiagram may be necessary to determine whether a given shadow is due to something within or just over the ureter. In the case of small stones, it is always well to cystoscope the patient and insert the ureteral catheter immediately before operation, in order to make sure that the stone has not passed into the bladder since the *x-ray* examination. The further limitations of radiography are shown by the fact that in almost 12 per cent. of Israel's cases, the picture was negative in spite of the presence of a stone. Its great value in positive cases, however, is not merely that it shows the *presence*, but also the *location* of the stone, thus permitting the exposure of the ureter to be limited to a comparatively short stretch. In *all cases*, Israel advocates *x*-raying *both kidneys and both ureters*, not only on account of occasional cases of contralateral pain, but of the not infrequent occurrence of a latent bilateral lithiasis (this was present in no less than 16 per cent. of Israel's series).

**INDICATIONS FOR OPERATION.** In view of the serious renal lesions which may result from an impacted ureteral stone on the one hand, and of the relative frequency with which such stones are spontaneously discharged on the other, the question of operative or expectant treatment is often puzzling. Israel's conclusions on this point are as follows: An *absolute* indication to operation is anuria for forty-eight hours; definite, but less urgent indications are bilateral lithiasis, and the combination of a ureteral stone and retention, with or without infection of the kidney. In a case of simple unilateral stone without complications, a waiting policy is to be pursued, unless (1) the stone is so large that its spontaneous passage is impossible, (2) characteristic pain, localized to a definite area, persists for a long time, or (3) repeated *x*-rays show no tendency of the stone to descend.

**OPERATIVE TECHNIQUE.** In all but a very few exceptional cases, *extraperitoneal* exposure of the ureter must be considered the method of choice, though in women the juxtavesical portion can often be satisfactorily reached through the vagina, provided the stone can be easily felt, and does not slide away. For intraparietally situated stones, the transvesical route must be adopted, usually by means of suprapubic, exceptionally by a vaginal cystotomy. The extraperitoneal exposure of the ureter is accomplished by Israel by means of his well-known incision, which follows a line from the junction of the twelfth rib and outer edge of the erector spinae muscles, obliquely downward to a point two finger-breadths to the median side of the anterior-superior spine, and thence bending slightly inward, runs parallel to Poupart's ligament, but two finger-breadths above it, to the median line. Only the particular

portion of this incision that is indicated by the situation of the stone is made. After dividing the structures of the abdominal wall, the peritoneum is reached, and is pushed medianward and upward, the ureter remaining attached to it in all cases where it is not fixed by inflammatory adhesions. After exposing the ureter, which at times may be accomplished with some difficulty, a light clamp is placed to each side of the stone, to prevent it from sliding away, and also to prevent escape of urine. An incision is then made over the stone, exactly parallel to the axis of the ureter, and the stone is removed. If possible, a single fine catgut suture is placed in the ureteral wall, but *not penetrating the mucosa*; if the wall is too thin to permit of this, it is not stitched at all, the periureteral fatty tissue merely being brought together over the line of incision. If none of this is available, the wound may be left to close without suture, which it will do in every case, without fistula formation, provided there is no obstruction to the ureter below. A small drain should be placed in the wound, but not touching the ureter.

In cases of severe and irreparable lesions of the kidney or ureter or both, nephrectomy is necessary, and the mistake should not be made of leaving a ureteral stone after the extirpation of the corresponding kidney, for subsequent colics may necessitate a second operation for its removal.

*Results.* Israel reports a mortality of but 3.7 per cent. (2 deaths) in a series of 53 operations for ureteral stone unassociated with anuria or urosepsis; of 6 cases *with anuria*, however, he lost 3; and of 2 cases with acute pyelonephritis and septicemia, he lost both, showing on the one hand, the extremely good prognosis in uncomplicated cases, the great danger, on the other hand, when they are allowed to go on to a condition of anuria or sepsis.

**Ureteral Injuries Following the Wertheim Operation.** The greatest single obstacle to the successful performance of any of the radical types of operation for uterine carcinoma is furnished by the *ureter*, since its close anatomic relation to the parametrium and cervix, and its liability to be firmly embedded in carcinomatous tissue, expose it to great danger of injury in the attempt to remove with the uterus any considerable amount of parametric tissue. It has been practically the universal experience that the more radically one operates, the greater will be the number of resulting ureteral injuries, such as fistulas and stenoses. Of considerable interest, therefore, is a review of the postoperative morbidity, with respect to ureteral lesions, occurring in the last 335 radical operations for carcinoma of the cervix performed in the Wertheim clinic, and reported by Weibel,<sup>1</sup> the first 400 cases having been previously reviewed in an earlier paper.<sup>2</sup> In both groups of cases, ureteral fistula occurred in about 6 per cent., and improved technique does not seem to

<sup>1</sup> Ztschr. f. Gyn. u. Urol., 1913, vol. iv, p. 138.

<sup>2</sup> Ibid., vol. Ixii, p. 184.

reduce this, although at times series of over 50 consecutive cases may be run without a fistula. The principal causes of fistula-formation are mechanical injury to the ureter during operation, and subperitoneal suppuration extending to the ureteral wall, the latter being responsible in only a small minority of cases, however; in many instances, on the other hand, extensive suppuration was present, but no fistula occurred. Moreover, complete isolation of the ureter from the surrounding tissue for a considerable distance resulted only a few times in fistula-formation; in the majority of cases where this did occur, the ureter had not been isolated. In a few instances, application of ligatures too close to the ureteral wall, with consequent kinking, may have been a causative factor, and very rarely unnoticed injuries to the outer coats during operation were probably responsible. It appears, therefore, that there is no uniform etiology for ureteral fistulas.

In the series of 335 operations, ureteral fistulas occurred 20 times. One patient died immediately after operation; in 7 the fistula healed spontaneously, and in 12 it did not heal. In 1 of the cases in which the fistula closed, complete occlusion of the ureter occurred, however, with elimination of the corresponding kidney.

With regard to the management of these cases, the author advises a long course of expectant treatment, operation being resorted to only after at least three months, unless beginning symptoms of an ascending infection force intervention earlier. When operation does become necessary, Weibel advocates nephrectomy in most instances as being simpler and less dangerous than the theoretically more ideal vesicular implantation of the ureter, but in the case of bilateral fistula-formation, implantation is of course the only operation to be considered.

The cases of spontaneous closure have been carefully followed, and in no instance has such a ureter, which showed good function at first, become obliterated subsequently, though once the reverse was true, a ureter which was for months absolutely closed showing after six years a distinct, though hyponormal functioning to the indigo-carmin test. In many cases which escaped fistula-formation, variations in ureteral functioning could be demonstrated months and years later, indicating the presence of constrictions, with resulting stasis. In the majority of cases, however, no such disturbances were encountered. In a few instances severe and even fatal ureteritis and pyelitis occurred after operation, without any fistula, these being probably the result of trauma to the ureter during operation.

In cases of actual injury to a ureter, recognized during operation, Weibel advocates suture if the wound does not exceed half the circumference; if more than this, implantation into the bladder should be done if possible; if not, nephrectomy is the only choice. The author is strongly opposed to *intentional* resection of the ureter, with implantation into the bladder, preferring to shell out an intact ureter from its carcinomatous

bed if necessary; in cases that have advanced to the point where the ureteral wall itself is actually invaded, thus *necessitating* resection, recurrence is practically sure to take place, and even the most radical type of operation offers no hope whatsoever.

**Accessory Ureter.** Hartmann<sup>1</sup> reports a case of the rather rare condition of an accessory, aberrant ureter in the female, opening just below the external urinary meatus, and causing the typical symptoms of slight, constant incontinence, accentuated by coughing, sneezing, straining, etc., but *associated with normal micturition*. This symptom-complex is so characteristic that it should at once arouse suspicion of the condition mentioned above, and yet most of these patients are treated for years in every possible way for a supposed sphincter insufficiency, without the slightest result. The tiny opening of the aberrant ureter may be exceedingly difficult to discover, but the diagnosis must finally depend upon its demonstration. Differential diagnosis between a fistulous tract communicating with the bladder and such an opening of an aberrant ureter is easily made as a rule by injecting colored fluid into the bladder. In only the exceptional case it is possible to pass an instrument of any sort into the aberrant ureter from below, on account of the small caliber and irregularity of the tract, or because of the presence of mucous folds. It may be exceedingly difficult or impossible to determine from which kidney the aberrant ureter comes, but this is of little practical importance—the main point is to determine that the trouble is in fact due to such an accessory ureter, and not to a mere vesical fistula, or to some form of insufficiency of the bladder muscle.

The only type of operation that comes into consideration in the treatment of the condition is some form of direct implantation of the aberrant ureter into the bladder. If the vaginal operation is performed, the surgeon must start at the external opening and follow the ureter wherever it leads him, whereas if he operates by the abdominal route, the relations are at once clear. Nevertheless, the author advocates the vaginal route, according to Franz's method, and was able by its means to produce a complete cure in the case which he reports.

**Physiologic Studies upon the Ureter.** Boulet<sup>2</sup> reports the results of physiologic studies upon the ureters of a man executed by beheading; the organs were removed twenty minutes after death, and were placed immediately in Ringer-Locke fluid. After about six hours the temperature of the fluid containing one ureter was raised to 40° C.; in about five minutes the ureter began making regular rhythmic contractions, each contraction lasting about nine seconds, followed by a pause of forty-one seconds. The second ureter was cut into three segments, and each studied separately. The renal segment, to which a small bit of the kidney pelvis was still attached, began contracting immediately,

<sup>1</sup> Ztschr. f. Urol., 1913, vol. vii, p. 429.

<sup>2</sup> Cptes. rend. hebdom. Soc. de Biol., 1913, vol. lxxiv, p. 1171.

about 15 times in eleven minutes. The other two segments also showed similar, but somewhat slower contractions, about 5 in eight minutes, and 4 in five minutes, respectively.

These experiments show that the human ureter, suspended in Ringer-Locke solution, is capable of rhythmic movements throughout its entire length, these being, to a certain degree at least, independent of stimuli coming from the bladder or kidney pelvis, because the isolated central segment showed the same type of contractions as the two ends. The renal segment showed, however, somewhat more rapid contractions than the other two.

The effects of adding to the Ringer-Locke solution various salts were also studied; barium chloride and calcium chloride were found to be powerful excitants, both to the rate and amplitude of contractions, whereas atropin and pilocarpin were practically without effect.

**Ureteral Prolapse.** A most remarkable case of extensive prolapse of the ureter, occurring in a girl, aged seventeen years, is reported by von Franqué.<sup>1</sup> She had been troubled with dysuria for six months, and had had some incontinence for eight days previous to coming under observation. Examination revealed an ulcerated and in part necrotic tumor the size of a walnut, hanging by a pedicle from the external urinary meatus. This was subsequently discharged while the patient was in bed, and on microscopic examination proved to be composed of completely necrotic tissue. Cystoscopic examination showed surrounding the right ureteral orifice a papillary mass, which the author took for a papilloma. On doing a suprapubic cystotomy for its removal, however, it was found that the ureter ran through its centre, and that it in fact represented a prolapsed and tremendously edematous portion of the ureteral mucosa. Under the guidance of a ureteral sound, introduced through the operative opening in the bladder, the mass was cut away, the ureteral and vesical mucosæ being united with a few fine sutures. Cystoscopic examination, three weeks later, showed a few bullous swellings around the right ureteral orifice, but this condition was much less marked than it had been at a previous examination, a few days after operation. Injection of indigo-carmin showed a regular rhythmic discharge of urine from this ureter into the bladder.

Microscopic examination of the specimen removed from around the ureteral orifice showed a very edematous connective-tissue stroma, containing a definite layer of ureteral muscle in the centre, and covered on one side by vesical, on the other by ureteral mucosa. At one point, the site could be determined from which the necrotic tumor, which had projected through the urethra, had been detached, showing that there had been a prolapse of the ureter, not only into the bladder, but *through the whole length of the urethra* as well, the tumor which had presented

<sup>1</sup> Monatssehr. f. Geb. und Gyn., 1913, vol. xxxviii, Ergzhft, p. 115.

outside the external meatus having been nothing more than a mass of greatly swollen, edematous, and necrotic ureteral mucous membrane.

**Incontinence of Urine.** In women of middle age there often occurs a troublesome incontinence of urine, which may be the result of child-birth, or may be unassociated with any demonstrable lesion of the urinary tract. The patient generally notices at first the occasional escape of a few drops of urine upon making any unusual exertion, this gradually growing worse until coughing, sneezing, lifting, or stepping up high is sufficient to cause a little urine to run out, and may finally end in more or less constant dribbling. The condition has usually been considered a very stubborn one, and many forms of operation have been devised for its relief, but as a rule without much success. Kelly<sup>1</sup> believes the key to the situation lies at the *internal sphincter*, and says he has succeeded by means of the following operation in relieving every case where no actual destruction of the tissue had taken place at the internal urethral orifice, *i. e.*, where there had not been a vesicovaginal fistula with sloughing.

**TECHNIQUE.** A Pezzer catheter, not over 5 mm. in diameter, is introduced into the urethra with the patient in the lithotomy posture. The posterior wall of the vagina is retracted, and the region of the vesical neck is brought down with forceps or by means of four guy sutures. The vaginal wall is then slit down to the urethra and bladder in the median line for about  $1\frac{1}{2}$  to 2 inches. The neck of the bladder should fall at about the centre of this incision. The position of the vesical neck is easily determined at all times by moving the catheter to and fro, and feeling its head, which presses close up against the urethra. Utmost care should be taken not to cut into the urethra or bladder. By means of blunt-pointed scissors, the vagina is now further dissected off on both sides for a distance of 2 to 2.5 cm. around the neck of the bladder, the dissection being deepest just at the region of the neck. When the detachment of the vagina from the bladder is complete, the finger should be able to grasp at least one-half to two-thirds of the vesical neck and contiguous portion of the urethra.

The next step is to suture together the torn or relaxed tissues at the neck of the bladder, using two or three mattress sutures of fine silk or linen, passed from side to side (Fig. 108). The first suture takes in about 1.5 cm. of the tissue, and is tied at once, when the succeeding sutures may be passed outside of this, thus further contracting and bringing together the tissues at the neck. The mushroom catheter is now pulled out, the head of the catheter escaping with a jump as it clears the tightened reconstructed sphincter. The more or less redundant vaginal walls are now resected, so that the remaining tissue can be snugly brought together to support the vesical area operated upon and prevent the formation of any dead space between the bladder and vagina.

<sup>1</sup> Urol. and Cutan. Rev., 1913, vol. xvii, p. 291.

**AFTER-TREATMENT.** No catheterization is performed unless it becomes imperative, though occasionally this may be necessary for several days. The patient should be placed on a Gatch bed in a half-sitting posture from the very first, and may be out of bed in a few days.

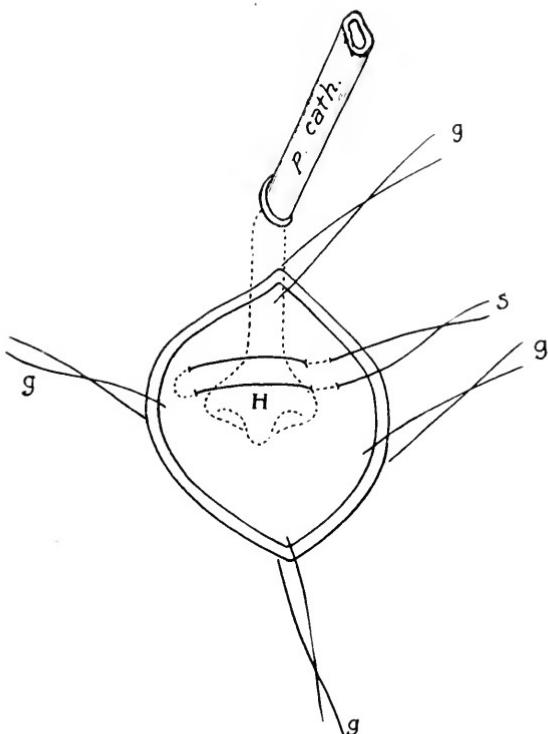


FIG. 108.—“*H*” is the head of the catheter, marking of the neck of the bladder. “*G*” are the guy sutures holding the wound open. “*S*” is the suture at the neck of the bladder, reuniting the sphincter muscle.

Worrall<sup>1</sup> has devised a somewhat similar operation for relief of the form of incontinence occurring in multiparae as the result of a dislocation of the urethra from its normal position beneath the pubic arch. Worrall thinks that in these cases the urethra has lost its normal curve, as a result of which the sphincter is placed at a great disadvantage in having to resist intra-abdominal pressure acting along a vertical axis. By advancing the meatus, the normal curve can be to a large extent restored; this is further aided by reattaching the neck of the bladder to the pubic arch by buttressing it up with fascia drawn from the sides. A diminution of the caliber of the urethra can be secured at the same time by forming a convex ridge on its floor, this also assisting in relieving the general relaxation.

<sup>1</sup> Journ. Obst. and Gyn. Brit. Emp., 1913, vol. xxiv, p. 225.

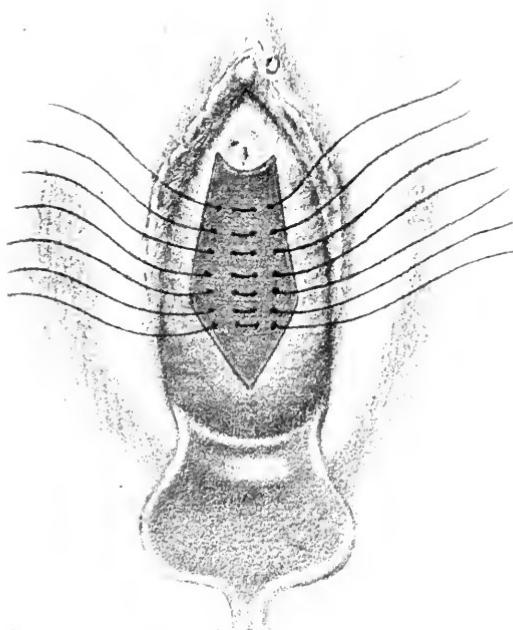


FIG. 109

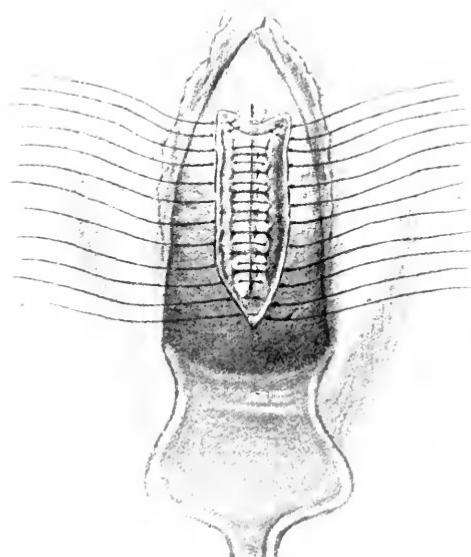


FIG. 110

The operation performed by Worrall consists in making a kite-shaped denudation, extending from the urethra nearly to the external os. Parallel sutures are then introduced as shown in Fig. 109, to form the projecting ridge on the floor of the urethra and neck of the bladder. After this first row of sutures has been tied, a second row is inserted, as shown in Fig. 110. The two anterior ones bring together the horns of the crescent semicircling the meatus, advancing this somewhat, while the remainder gather in the facia on each side, thus buttressing up the

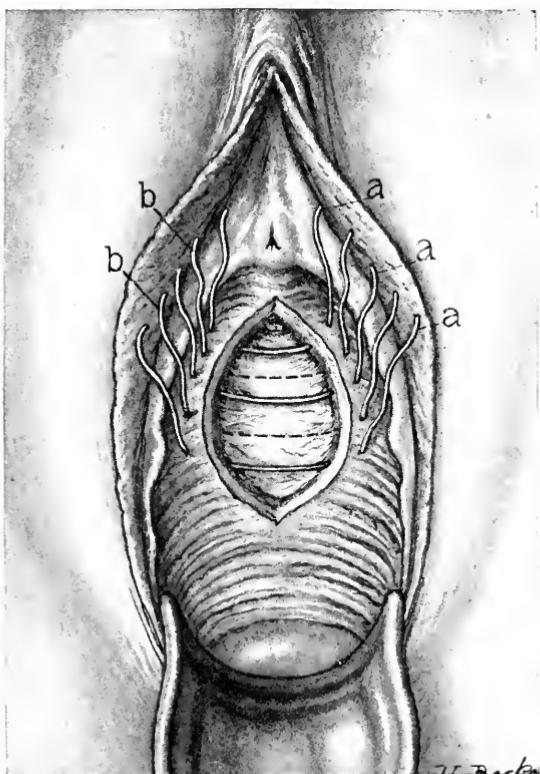


FIG. 111

urethra and neck of the bladder. In specially bad cases, the horns of the crescent should extend rather higher and nearer to the meatus. In addition, any relaxation of the pelvic floor or uterine displacement should of course be corrected.

The author reports 3 cases operated on by this technique with excellent results.

Baldy<sup>1</sup> describes an operation which he says has given him uniform

<sup>1</sup> *Surgery, Gynecology, and Obstetrics*, 1913, vol. xvii, p. 533.

satisfaction in a few apparently hopeless cases of complete, or almost complete incontinence, occurring postpartum. Its principle consists in making permanent pressure on the neck of the bladder and vesical end of the urethra by bringing together the vaginal mucosa, and underlying fibrous tissue, from each side so tensely as to cause firm compression in this region. This is accomplished by denuding the vaginal mucosa covering the neck of the bladder, carrying the denudation a half to

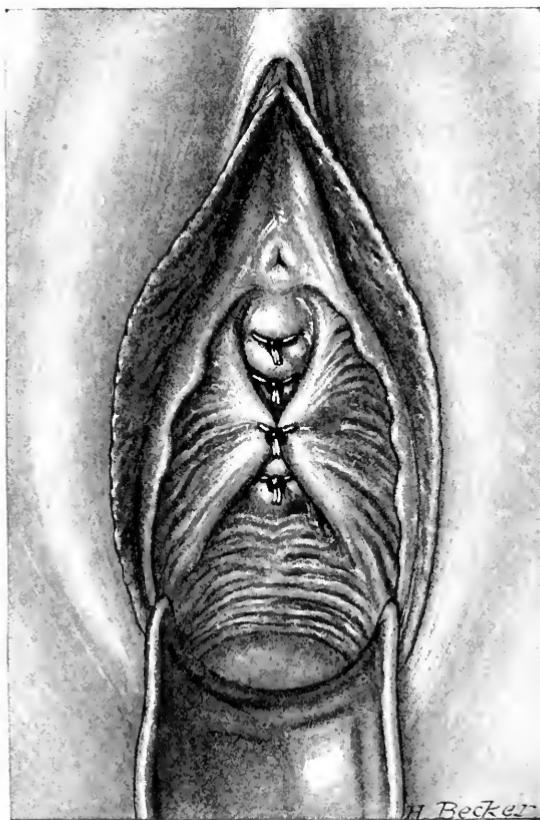


FIG. 112

three-quarters of an inch both anteriorly and posteriorly from the vesical neck, in order to insure full pressure at that point, the width of the denuded oval being limited only by the possibility of bringing the edges forcibly together with the aid of tenacula (Fig. 111). Actual resection of the submucous fibrous tissue is avoided, since the object is to double this tissue on itself, and thus obtain a firmer scar than would result if the redundant portion were resected and merely the comparatively thin edges brought together.

The stitches are interrupted, of silkworm gut. The first one is placed directly at the vesical neck, in the centre of the oval, care being taken to leave no blind space in the depth of the wound. After all the sutures have been secured, a reinforcing stitch is introduced (Fig. 112), the object of this being to draw the tissue from the extreme sides of the vagina over the line of sutures already placed, so as to relieve them of tension until healing is completed. This last stitch should therefore be placed well away from the first ones, directly at the point of greatest tension, the needle being introduced in the long axis of the vagina, so as to get an abundance of tissue, and passed as deeply as possible without perforating the bladder.

The subsequent treatment consists merely in keeping the sutures clean and dry; a permanent catheter is not used, but the patient should be catheterized several times in twenty-four hours. If a perfectly satisfactory result is not obtained the first time, the same process may be repeated, care being taken not to disturb any of the scar tissue from the former operation, so that the effect thus becomes cumulative, as it were. The author reports that this double operation was done in one exceedingly difficult case, with very gratifying end-results.

A somewhat different type of operation, but also having for its main purpose the production of pressure in the region of the vesical neck, has been practised by Steffeck<sup>1</sup> in 6 cases of bad incontinence associated with prolapse, 5 of these patients having practically no control whatever when on their feet. The method is practically a modification of the well-known Watkins' (or Schauta-Wertheim) operation of interposition for extensive prolapse.

Steffeck's technique is as follows: A curved incision, with the concavity upward, is made around the cervix immediately below the vesical attachment, and the bladder is thoroughly pushed off from the cervix and broad ligament. The free edges of the anterior vaginal wall are now caught with artery forceps and turned upward. The lower vesical attachment is separated with scissors from the vaginal wall, and the whole bladder pushed away by the gauze-covered finger from the anterior vaginal wall, being thus freed close up to the urethral opening; the operation must be so complete that no lateral bladder tags are left in place. The anterior vaginal wall is then split in the midline up almost to the urethral orifice. The peritoneum is now opened, and the uterus drawn forward, each tube being ligated close to the uterus, the author having found this a satisfactory method of assuring sterility, provided *silk* and not catgut is used. The uterus is then pushed back half-way into the abdominal cavity; the bladder is drawn forward with two forceps, puckered somewhat with a purse-string suture, and the vesical peritoneum attached with two catgut sutures to the posterior

<sup>1</sup> Ztschr. f. Geb. u. Gyn., 1913, vol. lxxv, p. 221.

surface of the *fundus uteri*, or in case of a very large uterus, directly on top of the fundus. The entire *posterior* surface of the uterus lies, therefore, *intraperitoneally*; the extraperitoneal top of the uterus is now fixed in the upper angle of the vaginal wound by two deeply placed silk sutures, and the operation completed by closing the anterior vaginal wall, including some uterine tissue in the sutures, the final step being the closure of the original incision around the cervix.

The result of this operation is that the bladder lies not *behind* the uterus, as in the ordinary Watkins' operation, but *above* it, where it can expand freely; by the fixation of the fundus immediately under the urethral orifice, moreover, a sufficient compression of the urethra is obtained to control the tendency to incontinence. The advantages claimed by Steffeck for this operation over the typical interposition one are that the position of the uterus is less radically changed, the dilatability of the bladder is in no wise restricted, and there is no diminution in the caliber of the vagina due to bulging forward of the uterine body, such as occurs in the Watkins' operation, and often leads to subsequent dyspareunia. The author says that the patients upon whom he has performed this operation have been permanently cured, and lead active lives, two of them being energetic horseback riders and tennis players.

**Hexamethylenamin as a Urinary Antiseptic.** Hexamethylenamin or urotropin is undoubtedly our most efficient drug for the treatment of infections of the upper urinary tract, but its antiseptic effect is produced only when the original substance is broken up into *formaldehyde* and *ammonia*, a process which takes place only in the presence of an acid urine. Some time ago Burnam<sup>1</sup> suggested a test for detecting formaldehyde in the urine, in order to control the extent to which the formation of this was actually taking place in any given patient to whom hexamethylenamin was being administered. It consists, briefly, in adding to a few cubic centimeters of warmed urine 3 drops of a 0.5 per cent. aqueous solution of phenylhydrazin hydrochloride, 3 drops of a 5 per cent. aqueous solution of sodium nitroprusside, and then an excess of warmed saturated aqueous solution of sodium hydroxide. In the presence of formaldehyde, in a strength of 1 to 20,000 or more an intense blue color is produced, gradually changing to green, and then to brown. In weaker solution, the blue stage is not seen, the first color being an intense green. Unsplit urotropin gives no reaction whatever.

Burnam was able to find formaldehyde in only about 30 per cent. of a series of urines tested, and thought that its production was due to a specific action of the renal epithelium.

In order to try out the accuracy and reliability of this test, G. G. Smith<sup>2</sup> has applied it to 213 specimens from 50 patients, and has come

<sup>1</sup> Trans. Amer. Urol. Soc., 1912, p. 286.

<sup>2</sup> Boston Medical and Surgical Journal, 1913, vol. clviii, p. 713.

to slightly different conclusions from those of Burnam. He has shown conclusively for one thing, by experiments *in vitro*, that urotropin may be split into formaldehyde and ammonia without the action of renal epithelium or of any enzymes, apparently as a result merely of the acidity of the urine. He has found formaldehyde present, moreover, in a much larger percentage of his cases than did Burnam, only one of the 50 patients tested failing to show at any time some formaldehyde elimination. He emphasizes in this connection that the urine should be examined as soon as possible after it has been voided, and that a negative test at one time does not prove that formaldehyde is never liberated. The activity of a urine in liberating it he found to be directly proportional to its acidity as shown by its hydrogen-ion content; the litmus paper test of reaction was unreliable in about 25 per cent. of the cases, however. In patients with a persistently alkaline urine, doses of boric acid, gr. x, t. i. d., proved moderately effectual in changing the reaction sufficiently to liberate formaldehyde, but sodium acid phosphate, in doses of one-half to one dram after meals, was even more efficient, when it did not cause too much diarrhea.

The tests have shown that a dose of urotropin, gr. v, may be followed by a positive formaldehyde reaction, but that this is very uncertain; gr. viij are nearly always followed by good quantities of formaldehyde, lasting six to eight hours, but a dosage of gr. x, every eight hours, or gr. xv, at 7 A.M. and 6 P.M., appears to produce the most satisfactory results.

Hinman<sup>1</sup> has also investigated this subject, and reports that experiments by himself and others have shown that formaldehyde must be present in any solution in a concentration greater than 1 to 30,000 to have any definite bactericidal effect, the best results being obtained with a solution of about 1 to 6000. To obtain this concentration in the urine, the drug must be given in large doses, at intervals of not greater than eight hours, and preferably oftener. Large amounts may be given with impunity, even as much as gr. xv, t. i. d., being in Hinman's experience too small a routine dose from which to expect a reasonably antiseptic effect in every case.

The larger the dose, the greater will be the concentration of the drug on excretion, but in addition to the dosage, there are numerous other factors affecting the results. The character of stomach contents is of some importance, in that the greater the gastric acidity, the larger will be the amount of hexamethylenamin broken up there, with corresponding loss for subsequent conversion in the urine. The degree of urinary acidity is the most important factor, and should always be greater than the equivalent of 2 c.c. of decinormal NaOII solution to 10 e.e. of urine. To increase the acidity of urines deficient in this respect, sodium acid phosphate was found by Hinman also to be the most satisfactory drug.

<sup>1</sup> Journal of the American Medical Association, 1913, vol. lxi, p. 1601.

The length of exposure of the drug to the influence of the urinary acidity is also of importance; in kidney affections moderate doses are of no value whatever, and in such conditions as cystitis or polyuria, with frequent micturition, time is not allowed for the conversion of the hexamethylenamin in the bladder into formaldehyde in amounts to be of antiseptic value. In addition to this, the higher the concentration of the drug, the more readily is it broken down, so that polyuria, causing dilution and lessened concentration, still further offsets the advantage of large doses. None of the proprietary substances analogous to hexamethylenamin were found by Hinman to have any greater antiseptic value than the pure drug itself.

#### MISCELLANEOUS TOPICS.

**Anesthesia in Gynecologic Work.** *Anoci-association.* In a paper read before the Gynecological Section of the American Medical Association at the Minneapolis meeting, Crile<sup>1</sup> discusses his well-known principle of "anoci-association" as applied to gynecologic work. Basing his theory on animal experiments, which show that identical brain-cell changes are produced by emotional excitation and by physical trauma under anesthesia, Crile has concluded that if all emotional stimuli associated with an operation could be reduced to a minimum, and the operation then performed so that no traumatic impulse could reach the brain, the dangers of the operation would be merely those which might result from the local injury, as all brain-cell exhaustion and its deleterious sequelae would be avoided. To this principle of eliminating all noxious or "noci-associations" he applied several years ago the term *anoci-association*; it includes a lessening of preoperative psychic strain by the use of appropriate drugs, the administration of a general anesthetic to obliterate all impressions during operation, the progressive use of local anesthesia during the operation to block off the passage of traumatic stimuli to the brain, and finally, the use of a local anesthetic of lasting effect, so that after-sensations of pain from wound-surfaces may be reduced to a minimum.

Crile's *technique*, as applied to abdominal and gynecologic work, is briefly as follows: One hour before operation the patient is given an injection of morphin gr.  $\frac{1}{6}$ , and scopolamin gr.  $\frac{1}{150}$ . Nitrous oxide and oxygen is the form of general anesthesia used, and is started in the patient's room if she is specially nervous. "Division of the tissue is preceded by nerve-blocking by means of the local administration of a 1 to 400 solution of novocain. Each division of tissue in the course of operation is preceded by infiltration with this local anesthetic, the block

<sup>1</sup> Journal of the American Medical Association, 1913, vol. lxi, p. 1501.

being made so complete that no nerve is left free to carry a single activating impulse to the brain. First the skin, then the subcutaneous tissue, then the fascia, and finally the remaining muscle or posterior sheath and peritoneum are in turn novocainized, subjected to momentary pressure to spread the anesthetic, and then divided within the blocked zone. The peritoneum is next everted, and a 0.5 per cent. solution of quinine and urea hydrochloride is infiltrated about the line of proposed sutures, and as before, the parts are then subjected to momentary pressure. This infiltration serves as a block, and as its effects last several days, it should prevent, or at least minimize the postoperative wound pain and shock. The quinin and urea salt cause a certain amount of edema of the tissue, which lasts for some time after the wound is healed. The following regions may be blocked in the same manner as the abdominal wall: the meso-appendix, base of the gall-bladder, uterus, mesentery, and any portion of the peritoneum. In performing a hysterectomy, the broad and round ligaments are thoroughly infiltrated with novocain before they are severed, and again before the wound is closed the stumps may be completely infiltrated with quinin and urea hydrochlorid, thus giving a degree of anesthesia for at least two days. The result is that the pulse rate at the end of the operations is the same as at the beginning, and postoperative rise of temperature, acceleration of the pulse, pain, nausea, and distention are minimized or wholly prevented."

According to Crile, not only is the postoperative morbidity greatly decreased by the adoption of this technique, but since its adoption by himself and his associates at the Lakeside Hospital in Cleveland, the average mortality has been very markedly reduced, as is shown by extensive statistics.

**Local and Spinal Anesthesia.** Gellhorn<sup>1</sup> is a strong advocate of *local anesthesia* in all manipulations about the cervix. He uses a 1.25 per cent. solution of novocain in normal salt, with a very small amount of adrenalin, injecting this at four points deep into the cervical tissue by means of a fine hypodermic needle; occasionally he injects small quantities of the solution around the periphery of the cervix and into the broad ligaments as well. It is rarely necessary to use over 10 c.c. of the solution all told. Gellhorn has found that with this technique dilatation of the cervix, curettage, amputation of the cervix, or trachelorrhaphy may be performed painlessly, and the method is of special value in removing adherent placental rests *post-abortum*; occasionally, however, it is necessary before curetting to insert a narrow strip of gauze, saturated with the novocain solution, into the uterine cavity for five minutes.

For more extensive operations, Gellhorn advocates *spinal anesthesia*, and says that he thinks the profession as a whole in this country, has

<sup>1</sup> Journal of the American Medical Association, 1913, vol. lxi, p. 1354.

been too quick to condemn it, on account of untoward results which have occurred in several instances, but which he believes are referable to the individual technique rather than to the method itself. He insists that the technique is of the greatest importance, and has found the following routine satisfactory in a fairly large series of cases, including a number of vaginal and abdominal hysterectomies and other major gynecologic operations:

The patient sits on the operating table, bent forward as much as possible; the lower part of the back is painted with iodin. The fourth lumbar spine is found by drawing an imaginary line between the crests of the iliac bones, this line crossing the vertebral column at the level of this spine. The needle is inserted just beneath the spinous process immediately above this (third lumbar) until a few drops of spinal fluid escape. A syringe is then attached, containing 3 e.c. of a 5 per cent. solution of novocain, with a few drops of 1 to 1000 solution of adrenalin. After allowing the solution and some of the spinal fluid to mix, the contents of the syringe are slowly injected into the spinal canal. The patient remains bent forward *for at least three minutes*, and is then *slowly* lowered to the dorsal position, the object of this being to prevent too rapid dissemination of the fluid to the higher centres.

Gellhorn has done altogether 63 operations according to this technique. In 1 case, in which stovain was used, analgesia was altogether insufficient, in 3 others, it was imperfect, and in 6 additional cases a few whiffs of ether had to be given on account of nervousness of the patient or length of operation, but in all the remainder there was complete absence of pain. In one case, the patient collapsed on being lowered to a reclining posture, but quickly responded to stimulant treatment. Vomiting took place quite frequently, especially when the peritoneum was incised, but never persisted. Severe headaches subsequent to operation, such as have been often reported, occurred in only one case; backache, on the other hand, in five. The author does not advocate using spinal anesthesia indiscriminately, and at present uses it on only about one-sixth of his cases, but he does think it is indicated in all cases with cardiac or pulmonary lesions, and in patients with a weakened general condition, and also in those with complicated conditions, in whom a severe and tedious operation appears probable. He does not agree with those who consider syphilis a contra-indication to spinal anesthesia.

Babcock<sup>1</sup> is likewise an enthusiastic advocate of spinal anesthesia, and is able to report personal experience with it in about 3000 cases, among which were 307 abdominal operations on the pelvic organs, and 254 vaginal operations involving the peritoneal cavity. Babcock now uses routinely the following solution: Stovain, 0.08 gm.; lactic acid, 0.04 e.c.; absolute alcohol, 0.2 e.c.; aqua dest., 1.8 e.c. This is

<sup>1</sup> Journal of the American Medical Association, 1913, vol. lxi, p. 1359.

put up in 2 c.c. ampoules, which are sterilized by the intermittent method at not over 65° C. He believes that this form of anesthesia is accompanied by much less shock during the operation than is inhalation narcosis, though it may accentuate preexisting shock, owing to the vasomotor relaxation which it produces. As a result of this action, hemorrhage is reduced to a minimum, but the author advises that spinal anesthesia be avoided or used with great caution in conditions of marked hypotension of the circulatory system. Where postoperative headache occurs, he thinks the solution used has been too old, and has undergone degeneration.

Babcock, although an ardent advocate of spinal anesthesia, and an extensive user of it in all his work, does not consider it a *universal* anesthetic. He does believe, however, that it produces the greatest amount of muscular relaxation with the least protoplasmic disturbance, and that while it is probably more dangerous than a short narcosis under ether or nitrous-oxide-oxygen, it is certainly safer than a prolonged narcosis, with complete relaxation, produced by either of these.

**Acromegaly and Ovarian Activity.** The extremely rare phenomenon of the occurrence of acromegaly following double oophorectomy has been observed by Goldstein<sup>1</sup> in a forty-eight-year-old woman, the eldest of a family of seven, all her brothers and sisters being normal and healthy. In 1903 the uterus and adnexa were removed on account of multiple myomas and menstrual disturbances. The patient had always been of rather large build, with heavy bones, but in the year following operation there occurred a gradual but marked increase in the size of the entire body, especially of the extremities, the face also becoming broader, and the chin more prominent. This was accompanied by subjective symptoms, such as occasional attacks of vertigo, great sensitiveness to slight degrees of heat or cold, vague pains, palpitation, etc. A definite increase in the size of the bones, especially of the extremities, was demonstrated by the x-rays, but there was no apparent increase in the size of the hypophysis.

There appears to be no doubt that the condition was a true acromegaly, coming on subsequent to castration. It can hardly be assumed, however, that the removal of the ovaries *alone* was the cause of this; the patient was from birth of larger and coarser build than her brothers and sisters, and it seems probable that she had a congenital tendency to gigantism, *i. e.*, that the delicate balance between the secretions of the ductless glands governing stimulatory and inhibitory functions with respect to growth were abnormally unstable, so that the removal of one important set of glands of internal secretion—the ovaries—was sufficient to upset this balance and cause hyperactivity of certain other glands, perhaps chiefly the hypophysis.

<sup>1</sup> Münch. med. Wochenschr., 1913, vol. lx, p. 757.

Bab<sup>1</sup> says that in his opinion acromegaly and osteomalacia are in a sense antagonistic processes, and that therefore ovarian secretion should neutralize an excessive activity of the hypophysis. Acting on this theory, he subjected a thirty-five-year-old patient, with well-developed symptoms of acromegaly and a demonstrable enlargement of the sella turcica, to an extended treatment with ovarian preparations. She was at first given daily fifteen 0.3 gram oöphorin tablets; this treatment was kept up for somewhat over a year, by which time the patient had taken over 5000 tablets. Marked improvement was noted—she felt much more active, her head was clearer, and she was able to do more work. During a part of the time, she was also given subeutaneous injections of 2 c.c. of a fluid ovarian extract (Ovarin Poehl), receiving in all 43 injections in the course of about eleven months. Each injection was followed for about twenty-four hours by sleepiness and a sensation of twitching in the hands and feet, but by the second day these had always entirely disappeared. A distinct reduction in the size of the hands, feet, and neck could be demonstrated, and a second  $x$ -ray, taken several months after the first, showed no further increase of the hypophysis.

Since there seemed to be no definite indication for an operation on the hypophysis, and since the continuous ovarian medication could hardly be kept up throughout the patient's entire life, an attempt was made to transplant a pair of ovaries removed from a woman suffering with osteomalacia. This was accomplished by means of an anterior colpotomy, the freshly extirpated ovaries being placed in subperitoneal pockets on each side of the cervix. For a time the patient felt remarkably improved, and said herself that she felt completely rejuvenated, but the improvement was only temporary, for about two and a half weeks after operation a piece of tissue, probably one of the implanted ovaries, was discharged from the vagina, and a few months later a tumor developed, which proved to be an inoperable rectal carcinoma, from which the patient soon died.

**Relationship between the Ovaries and the Thyroid.** As has been previously brought out in these pages, the idea is constantly gaining ground that the ovaries represent a link in the complicated system of ductless glands, whose various secretory products taken as a whole exert an important influence over various vital functions. It is also pretty generally believed that there exists between the ovaries and another representative of this group of glands—the thyroid—an especially close functional relationship, though there appears to be considerable difference of opinion as to the exact nature of this relationship, whether the two organs are antagonistic, compensatory, or complementary. A rather interesting attempt to explain the occurrence of certain types of so-called "idiopathic" uterine hemorrhage on the basis of a disturb-

<sup>1</sup> Zntlbl. f. Gyn., 1914, vol. xxxviii, p. 26.

ance of this ovary-thyroid relationship has been made by Schrt<sup>1</sup> who says that in 13 out of 20 cases of uncomplicated "metropathia," without anatomical changes, he found all the distinctive blood-phenomena which have been described by Kocher as characteristic of hypofunction of the thyroid gland (relative neutrophilic leukopenia, with corresponding lymphocytosis, in conjunction with a total leukocyte count of below 6000, and marked reduction in the coagulation time). In 6 of the remaining 7 cases the coagulation time was decreased, but either the neutrophilic leukopenia or the lymphocytosis was lacking. The author believes that disturbances in the relationship between the thyroid and ovary may perhaps be the cause of these hemorrhages, which have as yet remained unexplained on anatomic grounds, and that many cases of metropathia hemorrhagica may in fact be abortive forms of myxedema. Schrt also believes that a decreased functional activity of the thyroid may stand in a causal relationship to some cases of eclampsia.

Mannaberg<sup>2</sup> is such a firm believer in the close physiologic relation between the thyroid and the ovaries that he has gone so far as to attempt in 10 cases the treatment of exophthalmic goitre by *x-ray applications to the ovarian regions*. These were all ambulatory patients, whose manner of living was in no wise altered during observation, so that any changes noted must be considered due to the treatment itself. In practically all cases there was marked subjective improvement, a decided increase in weight occurring in 8 out of the 10, reaching in one instance to a fifth of the patient's original weight, and averaging over a tenth of this. The exophthalmos was reduced in half the cases, in one instance disappearing entirely, but in the other half it was unaffected. Practically no effect was produced on the size of the neck, some of the patients showing a slow increase, others a slow decrease.

The most marked improvement seen was in the subjective condition of the patients—with only one exception (a woman treated for only a short time) practically all symptoms disappeared, and the patients were able to return to their regular work, which had in most cases been interrupted. Diarrhea, which was present in several instances, disappeared after a few treatments. In 3 cases the irradiation of the ovaries was followed by exposure of the thyroid to the action of the rays, but a relapse occurred in 2 of these cases, and there was no improvement in the third. The author cannot speak of any complete *cures* as yet, although the treatment has been carried on for about a year and a half.

The effects noted are probably due, he thinks, to some quantitative or qualitative change produced in the internal secretion of the ovaries, such as the suppression of some substance formed in them which has been exciting the thyroid to the excessive production of something,

<sup>1</sup> Münch. med. Wochenschr., 1913, vol. ix, p. 962.

<sup>2</sup> Wien. klin. Wochenschr., 1913, vol. xxvi, p. 693.

the entrance of which into the circulation results in the symptom-complex characteristic of Basedow's disease.

**Fate of Spermatozoa in the Female Organism.** Although numerous statements have been made from time to time with regard to the length of time for which spermatozoa are able to retain their vitality in the female genital tract, practically no actual data have ever been presented with regard to this in the human species. In order if possible to throw some light on this subject, Holme and Behn<sup>1</sup> have carried out a series of tests of the vaginal secretions of a healthy primigravida of six months, with the following results: A specimen of secretion removed from the posterior fornix one-half hour after coitus was weakly alkaline, and contained a moderate number of actively motile spermatozoa, in conjunction with numerous dead ones; in a specimen taken fifteen minutes later only a few organisms showed a slight amount of motility, the majority being entirely lifeless. By one and a quarter hours after coitus the vaginal secretion had become strongly acid, and showed no living spermatozoa; after seven hours only comparatively few intact specimens were to be found, and all these were dead, but there were many rudiments—heads without tails, misformed heads, isolated tails, etc.

From these observations, it seems probable that an acid vaginal secretion is capable of killing practically all spermatozoa within one hour, a phenomenon which was confirmed experimentally by mixing on a warmed slide equal quantities of fresh seminal fluid with the strongly acid vaginal secretion of a nine months' pregnant woman; in every instance, all the spermatozoa lost their vitality within half an hour, whereas in control preparations they practically all retained their vitality for this period. Less strongly acid vaginal secretion from a non-pregnant woman took four hours to kill all spermatozoa, and a specimen of neutral secretion, from a menstruating woman, failed to accomplish this at all. Apparently, therefore, the spermatocidal action of the vaginal fluid is in direct proportion of its acidity.

With regard to the persistence of spermatozoa in the upper genital tract, the authors' experience is based on animal experimentation. They found that in guinea-pigs and rabbits both homogeneous and heterogeneous spermatozoa are largely, but not entirely destroyed in the uterus in two days; a few may persist till the fourth day, but by the sixth all living organisms have disappeared. These results agree fairly closely with a few published observations in human subjects, and it seems highly probable that the commonly accepted opinion that living spermatozoa, capable of fecundation, may persist in the upper genital tract for days or weeks is purely a myth, and that in all probability three days is the longest period throughout which such activity can continue.

<sup>1</sup> Zntlbl. f. Gyn., 1914, vol. xxxviii, p. 5.

In order to test the vitality of spermatozoa in the abdominal cavity, numerous experiments were made by injecting guinea-pigs intraperitoneally with human, ox, and guinea-pig semen, and examining the peritoneal fluid at various intervals. In all cases it was found that rapid destruction of the spermatozoa by active phagocytosis took place; this markedly inimical action toward spermatozoa on the part of the peritoneum justifies the conclusion that only in very rare instances does fecundation of the ovum take place by a spermatozoon which has passed through the tube into the abdominal cavity, although of course it cannot be denied that this may occasionally occur.

Waldstein and Ekler<sup>1</sup> have undertaken a series of experiments on 15 guinea-pigs, to determine by means of the Abderhalden reaction whether seminal fluid is in any way absorbed into the female organism. They first determined that normally no testicular antibody is present in the female guinea-pig blood. The same animals, however, after being covered, gave positive results, *i. e.*, their blood showed a specific reaction to testicular extracts, from which it must be assumed that following coitus a specific ferment is formed in the blood, with autolyzing activity toward seminal fluid. It would, therefore, seem that this must be absorbed into the vascular system of the female in a not entirely disintegrated state. In 9 out of 10 pregnant animals a similar reaction was obtained, though in a somewhat less marked degree.

**Intraperitoneal Hemorrhage from the Genital Organs, Unassociated with Pregnancy.** Notwithstanding the almost universally accepted idea that practically all intraperitoneal hemorrhages of genital origin in women are associated with an ectopic gestation, it should not be forgotten that cases occasionally occur of severe abdominal bleeding from the internal genitalia without a trace of any form of pregnancy having taken place. According to Gross and Heully<sup>2</sup> hemorrhage of this nature, unassociated with pregnancy, may occur from the uterus, tubes, or ovaries.

In a few rare instances, intraperitoneal hemorrhage may arise from the *uterus* as a result of the escape of menstrual blood through the tubes, in the presence of cervical stenosis, but a much more common source of such hemorrhage of uterine origin is the rupture of venous sinuses about fibromyomas; a number of such cases are on record, and in at least one of these the hemorrhage was so severe as to cause death. This phenomenon is easy to understand when one considers the extremely rich vascular supply on the peritoneal surface of such tumors, and the engorgement and friability of the veins. In some instances, spontaneous rupture may occur, in others, slow trauma, or a twist of the tumor on its pedicle may be the causative factor.

When hemorrhage comes from the *tube*, in the vast majority of cases

<sup>1</sup> Wien. klin. Wochenschr., 1913, vol. xxvi, p. 1689.

<sup>2</sup> Arch. mens. d'Obst. et de Gyn., 1913, vol. iii, p. 462.

a tubal pregnancy is of course responsible, though a few undoubted examples have been observed of so-called "tubo-ovarian varicocele," with hemorrhage from the enormously distended and varicose veins of the broad ligament, unassociated with pregnancy.

A very slight amount of hemorrhage comes from the *ovary* with each rupture of a Graafian follicle, but this is so slight as to be of no clinical significance. Occasionally, however, severe intra-abdominal hemorrhage may occur from a ruptured Graafian follicle in an ovary that is apparently normal in every respect, and shows no trace of inflammation, tumor formation, or pregnancy. Such a case is reported by the authors. A laparotomy was performed on a woman, aged thirty-seven years, on account of sudden, severe pains in the left ovarian region. On opening the abdomen, about 400 grams of uncoagulated blood were found in the peritoneal cavity; both tubes and ovaries were normal in size, but the left ovary showed an irregular laceration, about 1 cm. in diameter, to whose edges a few blood clots were adherent. On making serial sections of the entire ovary, this region was found to be intensely congested and hemorrhagic; the hemorrhage was of follicular origin, but no inflammation or chorionic villi were found. Similar cases of hemorrhage, arising from the corpus luteum menstrualis, have been observed. More often, however, non-gravid ovarian hemorrhage is associated with some pathologic condition of the organ, such as follicle cysts which become hemorrhagic and rupture, usually as the result of some slight trauma, or from overdistention.

# DISEASES OF THE BLOOD. DIATHETIC AND METABOLIC DISEASES, DISEASES OF THE THYROID GLAND, NUTRITION, AND THE LYMPHATIC SYSTEM.

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## THE BLOOD.

**General Considerations.** In a research on "The Rate of Reproduction of the Various Constituents of the Blood," O'Brien,<sup>1</sup> after taking 10 liters of blood from an immunized horse, noted the following: The number of white cells varies widely and irregularly. Very small differences are found in the differential count. The hemolytic titer remains practically constant, showing variations of at most 10 per cent. from the initial figure. The total amount of salts present does not decrease but may be increased 10 per cent. The content of all other blood constituents falls, the hemoglobin and number of red cells falling together to 50 or 60 per cent. of the initial figure. The color index of the new red cells remains at the normal figure. The curve of volume of the red cells does not correspond very closely with that of the number of red cells. The curves of total proteins and of diphtheria antitoxin show a fairly close relationship.

The effect of high altitudes upon the constituents of the blood has received more than usual notice in the literature of the year. From an elaborate piece of work taken up by Laquer<sup>2</sup> on this subject, the conclusions given were: (1) In a healthy young man who spent four weeks at an altitude of 2900 meters, there was an increase in the volume of erythrocytes and hemoglobin. This began slowly in the second week, and in fifteen days reached its height of plus 15 per cent. for the erythrocytes and plus 16 per cent. for the hemoglobin. After that the values remained stationary. The curves for these constituents ran parallel. (2) After return to low levels the hemoglobin and erythrocytes gradually receded in the course of three weeks to the original values. (3) This relative increase in the capillary blood corresponds to an increased blood formation. (4) After active exercise in high altitudes there occurs a decrease in the blood concentration in the finger tip,

<sup>1</sup> Journal of Pathology and Bacteriology, Cambridge, July, 1913, vol. xviii, No. 1.

<sup>2</sup> Deut. Arch. f. klin. Med., 1913, vol. cx, p. 189.

which is apparently due to vasomotor phenomena. (5) Six dogs at an altitude of 2900 meters which were bled to the extent of one-half their blood volume showed a return of the constituents of the blood to normal in sixteen days (average). After the same amount of bleeding at low levels, four of these dogs and two others showed a return to normal twenty-seven days (average). (6) High climates specifically stimulate new blood formation, and this is probably due to the lower partial pressure of the oxygen.

Cohnheim and Weber<sup>1</sup> have examined the blood of twenty-three persons engaged for long periods of time in operating the railway ascending the Jungfrau. Most of these subjects spent a great deal of their time at altitudes varying from 2300 to 3450 meters. They found values for both the erythrocytes and hemoglobin which were much higher than the normal at sea level. Cohnheim believes that these high figures obtained from subjects accustomed to living at high atmospheric levels leave no alternative but to assume a new formation of erythrocytes under such conditions.

Bürker,<sup>2</sup> after a very careful investigation, using every precaution to avoid experimental error, found that high altitudes unquestionably influence the blood as to the number of erythrocytes and the percentage of hemoglobin. The increase in these constituents is not only relative but absolute. The erythrocytes showed an increase of from 4 to 11.5 per cent., and the hemoglobin one of 7 to 10 per cent. The qualitative examinations showed that oxyhemoglobin was the only hemoglobin derivative concerned in the increase. He found that the increase of these constituents took place promptly on ascending to higher levels, but on returning toward sea level the blood does not resume its normal composition so promptly. In this connection, it is interesting to note Schneider's<sup>3</sup> observations on a man who had been resident manager of the Summit House on Pike's Peak (14,000 ft.) for seventeen years. On his descent from the Peak after a stay of six months, the hemoglobin showed a very slow decrease. In the first thirty days the percentage fell from 148 to 132, and during the following six weeks it dropped to 122. The erythrocytes decreased from 7,700,000 to 7,000,000 in this time.

Against the theory of increased formation of the red cells, Lope<sup>4</sup> quotes from a number of writers, and cites his own experiences, which seem to show that the dry, rarefied air of high altitudes dries out the blood so that the apparent increase in the number of corpuscles is merely a matter of greater concentration, and not an increased production on the part of the blood-forming organs.

<sup>1</sup> Deut. Arch. f. klin. Med., 1913, vol. ex, p. 225.

<sup>2</sup> Zeit. f. Biol., 1913, vol. lxi, p. 379.

<sup>3</sup> American Journal of Physiology, 1913, vol. xxxii, p. 295.

<sup>4</sup> Semana Medica, Buenos Aires, 1913, vol. xx, No. 19.

Fowell,<sup>1</sup> in a research on the iron in the blood, found that, in all individuals, there is an excess of this constituent over that which is combined with hemoglobin. In normal persons such excess bears a varying ratio to the total amount of iron, but such variation is within definite limits, averaging 4.2 to 1. In simple secondary anemias, this is also true, but the ratio is, on the whole, a little higher, averaging 3.7 to 1. In pernicious anemia the ratio is markedly elevated, approaching 2 to 1. In cirrhosis of the liver there is no excess of iron in the blood, and the ratio lies within normal limits.

**Blood Platelets.** From his investigations, Brown<sup>2</sup> concludes that, under normal circumstances, blood platelets are largely derived from the megakaryocyte of the blood-forming organs. The transitional leukocyte, which represents a persistent form of the embryonic pre-megakaryocyte, is a circulating homologue of the megakaryocyte and probably plays some part in normal platelet formation. When there is an excessive demand on platelet production, there may be a greater or less reversion to an embryonic mode of platelet formation in which less highly specialized cells than the megakaryocyte participate in the production of platelets. Besides the megakaryocyte, other cells have been found to take part in the formation of platelets. These are the hyperplastic endothelial cells in the marrow, and the mononuclear and transitional cells (pre-megakaryocytes) in the marrow, the spleen, and the blood.

Duke<sup>3</sup> has carried out a series of experiments on rabbits with the view of ascertaining what effect various injections of diphtheria toxin, benzol, and tuberculin would have on the blood-forming organs, and especially on the blood platelets.

The author's conclusions from these experiments are as follows: Diphtheria toxin in large doses is immediately poisonous to the bone marrow—possibly also to the platelets themselves—and causes an immediate fall in the platelet count.

Benzol in large doses, and diphtheria toxin in sublethal doses, act first as stimulants, and then as poisons to the platelet-forming tissues and cause thus first a rise and later a fall in the platelet count. It is possible that the platelets themselves are also affected by these agents, and that this contributes to the change in the counts.

Tuberculin in large doses, benzol in small doses, and possibly also diphtheria toxin in very small doses, act for a certain period of time only as stimulants to the progenitors of the platelets and cause only a rise in the platelet count.

It is believed that both the high counts and the low platelet counts observed in humans with diphtheria are caused by the action of varying

<sup>1</sup> Quarterly Journal of Medicine, January, 1913, vol. vi, No. 22.

<sup>2</sup> Journal Experimental Medicine, New York, September, 1913, vol. xviii, No. 3.

<sup>3</sup> Archives of Internal Medicine, January, 1913.

amounts of one and the same agent—diphtheria toxin. Low platelet counts in this disease would indicate a more severe toxemia than high counts, and low counts early in the disease a more severe case than low counts late in the disease. This reasoning it is believed may apply to other diseases also, and would seem to account for the occurrence of high platelet counts and low platelet counts in the same pathologic conditions.

It has been suggested by several observers that a poverty of the blood in platelets plays a role in the pathogenesis of purpura hemorrhagica. The work reported here supports this view. Purpura hemorrhagica of a certain type was observed in every instance (human and experimental) in which the platelet count descended to a certain low level.<sup>1</sup>

The view expressed by the author in a previous paper that platelets were probably very short-lived bodies, harmonizes with the results reported here, and it is believed accounts for the fact that the platelet count can rise and fall with such rapidity.

**Erythrocytes.** Butler<sup>2</sup> has made an extensive study of the fragility of the red-blood corpuscles. In reviewing the investigation as a whole, the author looks upon the results as somewhat disappointing owing to their negative character, especially in the various pathological conditions where positive results were expected. The fragility of the red-blood corpuscles appears to be extraordinarily constant in normal and pathologic conditions. From his work, the following conclusions seem to be justified: The minimum resistance of the normal red corpuscle, when examined as blood, is shown as commencing hemolysis in 0.375 per cent. to 0.4 per cent. sodium chloride solution when a one in ten dilution is used. The resistance of washed red corpuscles is normally less than that of the unwashed corpuscle, the minimal resistance being obtained in a salt solution of 0.425 per cent. to 0.45 per cent. sodium chloride solution. The necessity of employing a constant dilution of blood in recording results in order that they may be comparable has been demonstrated, and the lack of this precaution is the cause of discordant results of other observers.

The rapidity with which washed red corpuscles in normal saline alter their resistance has been shown, and the necessity of experiment being continued with freshly washed red corpuscles has been pointed out. Such deterioration is not demonstrable in red corpuscles kept in citrated plasma from twenty-four to forty-eight hours. Different anti-coagulants may be used, except leech extract, without altering the red corpuscle fragility, provided the red corpuscles are subsequently washed with normal saline solution.

Oxygen is capable of decreasing the fragility of the red-blood corpuscle. Carbon dioxide has a very marked effect in increasing the

<sup>1</sup> See PROGRESSIVE MEDICINE, June, 1913, p. 301.

<sup>2</sup> Quarterly Journal of Medicine, London, January, 1913, vol. vi, No. 22.

fragility, and these two effects are interchangeable. The decreased fragility of the red-blood corpuscles in obstructive jaundiced conditions has been confirmed. The increased fragility of the red corpuscles in congenital acholuric jaundice is confirmed. The effect of oxygen and carbon dioxide on these corpuscles has been shown not to differ from the effect on normal corpuscles. A slightly decreased fragility of the red corpuscles has been demonstrated in pyenia, septicemia, pneumonia, and chronic tubal nephritis. An increased fragility is shown in cyanosed states. Fragility appears to be normal in erysipelas, scarlet fever, Graves' disease, carcinoma, syphilis, general paralysis, tabes, chlorosis, pernicious anemia, myelemia, lymphemia, purpura, paroxysmal hemoglobinuria, and malaria. The fragility of the red corpuscles in diabetes appears to vary considerably. The effect of ingestion of sodium chloride has been noticed to decrease the fragility of the red corpuscles.

The resistance of reticulated erythrocytes has been investigated by Pepper and Peet.<sup>1</sup> In discussing their results, they say that of the anti-erythrocytic phenomena demonstrated by vital staining, that one known as reticulation of the erythrocytes is the most important. This reticulation may be briefly described as an intra-erythrocytic phenomenon demonstrable only by vital staining with a basic dye, occurring in a small percentage (0.5 per cent.) of the erythrocytes of the normal blood, and in much larger percentages in many pathologic conditions. Its distinctive structure is suggested by its various names and is quite variable, sometimes being only a few granules connected by fine threads; at other times a network of threads with many granules, and again, a thick ball-like tangle of threads. Its appearance is always characteristic, and it cannot be confused with any of the other basophilic changes in the erythrocytes. It may be demonstrated either in wet, vitally stained preparations, or in vitally stained preparations which can later be fixed, and which may be counter-stained with Giemsa's or Wright's stain. This reticulation is an evidence of youth of the cell.

A study of the literature of the subject leads to the belief that reticulated erythrocytes show greater resistance to hemolytic agents than do unreticulated forms. No consistent satisfactory proof of this has, however, been presented. The authors' experiments have failed to demonstrate any constant difference between the resistance of the reticulated and non-reticulated erythrocytes of rabbits' blood under normal and experimental conditions.

The cause of rouleaux formation by human blood corpuscles has been studied by Wiltshire.<sup>2</sup> He says that the lack of an exact method of measuring the degree to which rouleaux formation is present makes

<sup>1</sup> Archives of Internal Medicine, July, 1913,

<sup>2</sup> Journal of Pathology and Bacteriology, Cambridge, January, 1913, vol. xvii, No. 3.

the study of this phenomenon in disease most unsatisfactory. It is stated to be deficient in all forms of anemia, in Raynaud's disease, and in sunstroke; and increased in all forms of suppuration, pneumonia and acute rheumatism, owing to increase in power of the serum. Wiltshire obtained definite results in pernicious anemia only. Six cases were examined, and, in five, rouleaux formation was found to be distinctly defective in fresh films. On examination of the serum and washed corpuscles separately, this deficiency was found to be due to some fault in the corpuscles. The sera of these cases formed rouleaux well with normal corpuscles, but each serum was practically inert with its own corpuscles. Further, the corpuscles of these cases formed very poor rouleaux with normal serum. The sixth case seemed to be exceptional, good rouleaux being formed. Poikilocytosis will not account for deficiencies on the part of the corpuscles, since it may be present to a marked degree in other types of anemia which show good rouleaux formation.

The results of Wiltshire's experiments are summarized as follows:

- (1) The viscosity of the fluid medium in which red corpuscles are suspended exerts a slight influence on rouleaux formation.
- (2) Certain colloids, such as gum, will cause formation of rouleaux of red corpuscles.
- (3) Serum or pathologic fluids which will form rouleaux lose their power when diluted to a slight degree.
- (4) Blood-serum rapidly loses its power to form rouleaux when kept, but the rate at which this change takes place is subject to considerable variation.
- (5) The same may be said of the corpuscles.
- (6) The effect of temperature on "serum body."
  - (a) "Serum body" is probably not injured by a temperature of 100° C. acting for fifteen minutes.
  - (b) The power of serum appears to be increased by exposure to 60° C. for fifteen minutes.
  - (c) The loss of power of serum when kept is delayed by heating to 60° C. for fifteen minutes.
  - (d) Serum which has lost power completely does not regain it when heated to 60° C. for fifteen minutes.
  - (e) "Serum body" is not injured by freezing.
- (7) Saturation. In this respect "serum body" does not react like hemagglutinin. Pathologic exudates.
- (a) Inflammatory exudates have very marked rouleaux-forming power.
- (b) Passive exudates are weak or powerless.
- (c) Both retain their power when kept.
- (d) The marked power of inflammatory exudates is not related to activity on the part of any special type of cell.
- (9) Injuring cells or keeping them in contact with serum does not appear to influence the power of that serum.
- (10) Certain bacteria, when grown in serum, cause a marked power for rouleaux formation to appear. Other bacteria are inert in this respect. Iso-agglutinin is unaffected by these bacteria.
- (11) Red corpuscles lose their power to form rouleaux when subjected to comparatively low degrees of heat (38° to 45° C.).
- (12) The corpuscles also lose this power under the influence of carbon dioxide and hydrogen, possibly owing to reduction

of their hemoglobin. Conversion of oxyhemoglobin into CO-hemoglobin makes no difference. (13) Simple alterations of the acidity or alkalinity of the medium surrounding red corpuscles makes no difference in rouleaux formation. (14) The serum of cases of pernicious anemia possesses normal rouleaux-forming power. The decrease in power seen in this disease is due to some change in the corpuscles. (15) Rouleaux formation is a constant occurrence in normal shed blood.

**Leukocytes.** Fiske<sup>1</sup> has investigated the *diagnostic significance of the leukocyte count in osteomyelitis and tuberculosis of bones in childhood*. In his routine examination of children with tuberculosis of the bones and osteomyelitis, two-thirds of the cases in both diseases being in an acute stage, there was shown an average white count of 11,600 for the former, and 16,200 for the latter, a significant difference of about 5000 leukocytes. He considers this difference constant, and a useful factor in diagnosis from the fact that in osteomyelitis but 24 per cent. of the counts were below 12,000 as compared with 66 per cent. in tuberculosis; while 39 per cent. of the former were over 18,000, and but 13 per cent. of the latter over 15,000. This difference is still more emphasized in the acute cases which largely make up those seen in hospital practice. 22,200 was the average for osteomyelitis in this class, and 11,400 that for tuberculosis, a difference of nearly 11,000.

The Arueth method of counting the leukocytes has been received with some favor in this year's literature as a prognostic procedure. Cummings<sup>2</sup> and Holroyd<sup>3</sup> both report upon it favorably. Bonsdorff<sup>4</sup> has written a monograph of 206 pages on the subject.

Carles and Laurice<sup>5</sup> are convinced that the *fragility of the leukocytes* is an important *index of the resisting powers of the organism* and is thus useful for prognosis in many conditions. They agree with Feuillie that albuminuria in some cases is less a result of pathologic conditions in the kidney than of lessened powers of resistance in the blood corpuscles, particularly the leukocytes.

In their study they report their observations in fourteen cases of nephritis, seven cases of pneumonia, cases of diphtheria, acute rheumatism, and typhoid fever, in addition to those in two healthy persons. They estimate the number of apparently sound and destroyed leukocytes in the smear, counting across the field in a straight line. In health, the broken-down leukocytes amount to about 7 per cent., while in nephritis there may be 40, or even 64 per cent. The larger the number of destroyed cells, the more severe the impairment of health. All their

<sup>1</sup> Boston Medical and Surgical Journal, April 24, 1913, vol. clviii, No. 1.

<sup>2</sup> California State Journal of Medicine, July, 1913, vol. xi, No. 7.

<sup>3</sup> British Medical Journal, London, May 3, 1913.

<sup>4</sup> Kurt Kabitsch, Würzburg, 1913, Publisher.

<sup>5</sup> Journal de Médecine de Bordeaux, May 4, 1913, vol. xliv, No. 18.

work was done on adults. The technique is simple. A solution is employed containing 6 grams of sodium citrate and 67 grams of sodium chloride to the liter of water. 20 drops of this and 10 drops of distilled water are mixed, and to this mixture a drop of the blood is added. After twenty minutes, this is centrifugated, and the sediment spread on a slide by means of cigarette paper held by one edge and resting its weight at the other end of the specimen. This becomes an easy procedure after a little practice, and allows instructive comparisons to be made between the albumin, the amount of urine, the temperature, and the fragility index.

Aschenheim<sup>1</sup> makes an interesting suggestion on the basis of the study of the *effect of the sun's rays on the leukocyte count*. The author subjected 31 patients to a blood count before and after an hour's exposure of the body to the direct action of sunlight. 80 per cent. of these showed a general leukocytosis in the peripheral blood, with a relative increase in lymphocytes and a decrease in polymorphonuclears. Lymphocytosis being regarded by many as a defensive reaction against tuberculosis, the author wonders whether this may not account for the favorable effect of sunlight on the disease.

Chuprin<sup>2</sup> finds that eosinophilia occurring in the blood and sputum in cases of tuberculosis of the respiratory tract may be of diagnostic and prognostic importance. In favorable cases, the eosinophiles in both blood and sputum are increased in number. He cites a number of cases showing marked increase in these cells when the patient's health was improved, and either an absence or marked decrease when the disease was aggravated. Diminished number of eosinophile cells in the blood may indicate a spreading of the process, or a possible secondary infection. In the author's opinion, eosinophilia is due to the same factors in tuberculosis as it is in emphysema, asthma, and acute and chronic bronchitis, that is, a lack of oxygen and consequent chronic asphyxia, the result being decomposition of hemoglobin.

EFFECT OF CROTALIN ON THE BLOOD. Spangler<sup>3</sup> has studied 252 cases of *epilepsy treated by injections of crotalin*. In 161 of these cases complete blood counts were made after the administration of crotalin solution for periods of from two to six months. In this series he found that the injections had no influence on either the erythrocytic, the leukocytic, or the hemoglobin counts. The author says that while crotalin does not produce a leukocytosis, it does have a marked influence on the differential count. Careful records were tabulated in 57 cases in which from 6 to 12 or more differential counts were made over periods of from three to six months in each case. This series showed that crotalin has a decided tendency to produce an eosinophilia; and, more-

<sup>1</sup> Zeit. f. Kinderheilkunde, Berlin, 1913, vol. ix, No. 2.

<sup>2</sup> Medizinskoe Obozrienie, Moscow, 1913, vol. lxxix, No. 1.

<sup>3</sup> New York Medical Journal, October 4, 1913, vol. xcvi, No. 14.

over, the susceptibility of the individual to crotalin can be determined by the degree of eosinophilia produced. From forty-eight to seventy-two hours after an injection of crotalin solution, depending upon the susceptibility of the patient, the proportion of eosinophiles will often be increased from 8 to 10 per cent. In more susceptible individuals they are often increased to 15 or 20 per cent.; while in patients showing oversusceptibility, the author has seen as much as 30 per cent., and, in one instance, 43 per cent. of eosinophiles present.

Crotalin, as used in these cases, has acted as a foreign proteid. The interval between the injections was of sufficient length to sensitize the organism and to produce an anaphylactic state, and it is altogether possible that this eosinophilia is but an expression of anaphylaxis.

Ahl and Schittenhelm<sup>1</sup> have carried out a series of experiments on guinea-pigs into which they injected various proteid substances in order to sensitize the animals. They found, upon injecting the second dose after sufficient interval, that the resulting reactions were accompanied by various degrees of eosinophilia. In their experiments, they used albumin, fibrin, and globulin, and, on re-injection, eosinophilia was found. With nucleoprotein, histon, and caviar peptone, high grades of eosinophilia were produced. On the other hand, other protein end-products, such as nucleic acid and protamin, produced but a slight increase, if any, of the eosinophiles.

The authors concluded, from their experiments, that there is a marked difference in the power of different proteids to produce eosinophilia, and they suggest that this property belongs to a class of substances with certain distinctive chemical structure; and that anaphylaxis is not due to a certain, definite, single poison, but to a group of chemically related substances.

Herrick<sup>2</sup> has used an extract of the bodies of *ascaris lumbricoides* in sensitizing guinea-pigs. The aims of his experiments were to find (1) whether eosinophilia of the blood could be produced experimentally by the use of such an extract; (2) under what conditions of administration of this extract such eosinophilia might be brought about; (3) whether or not the substance influencing the eosinophiles is a protein; (4) whether such eosinophile increase bears any relation to specific sensitization or anaphylaxis. Throughout his work the author kept in mind the possible relation of these questions to the clinical problem of bronchial asthma. His results show that a notable eosinophilia of the blood can be developed by the intraperitoneal injection of an aqueous extract of *ascaris lumbricoides*. He found that when the injections were made at short intervals no eosinophilia or other phenomena resulted; but when made at intervals of from five to twenty-five days, a marked eosinophilia resulted from a single injection, while

<sup>1</sup> Ztschr. f. gesamt. exper. Med., 1913, vol. i.

<sup>2</sup> Archives of Internal Medicine, February, 1914, xi, No. 2.

in some instances death from acute shock followed the subsequent injections. The substance causing such eosinophile increase he found to be protein; afterward, when the extract was rendered protein-free by precipitation and filtration, no eosinophilia resulted from its introduction into the previously sensitized guinea-pigs. Previous sensitization is necessary to the development of this eosinophilia, and it is impossible to produce such eosinophilia while the animals are immune to the extract. This phenomenon of eosinophilia may, therefore, be considered evidence of previous sensitization, and Herrick suggests that there is a possible association of these facts with the problem of bronchial asthma.

Schlecht<sup>1</sup> has found that parenteral injections of a foreign proteid given at long intervals produces an experimental eosinophilia in guinea-pigs. This eosinophilia is both general in the blood and local in the peritoneum. The true proteins, as well as the lower proteins down to the peptones, are proved to be active in this respect. The lower protein end-products (amino acids) are inactive. The principal source of the eosinophilia lies in an increased formation of cells in the bone marrow, and an increased outflow of these into the circulation. The author holds that this experimental eosinophilia following an injection of foreign proteids is related to the phenomena of anaphylaxis and immunity. He believes this eosinophilia to be a protective reaction of the body against the invasion of foreign proteids and also against the toxic products resulting from the abnormal destruction of autogenous products. He suggests that there is a far-reaching similarity between the anaphylactic state and bronchial asthma.

Steiger and Strelbel<sup>2</sup> have found a local secretion eosinophilia to be a constant accompaniment of spring catarrh, as well as a general blood eosinophilia ranging from 5 to 21 per cent. The amount of the general eosinophilia and the grade of the local secretion eosinophilia appear to be in direct proportion and the secretion eosinophilia is a consequence of the primary blood eosinophilia. They call attention to the analogy which exists between spring catarrh and hay fever, and believe that both of these diseases are due to an oversusceptibility to an unknown toxic factor borne by the air.

Hoesslin<sup>3</sup> has been classifying all his cases in the last two years in which there was manifest lymphocytosis, restricting this term to the cases in which there were 30 or more lymphocytes to each 100 leukocytes. He found 100 patients with this lymphocytosis, absolute in 71 cases, that is, with more than 2000 lymphocytes to the cubic millimeter. The blood findings were kept under frequent control; when there was

<sup>1</sup> Archiv f. exper. Path. u. Pharm., 1913, vol. lxvii, p. 137; see PROGRESSIVE MEDICINE, June, 1913, p. 296.

<sup>2</sup> Zentralbl. f. inn. Med., 1913, vol. xxxiv, No. 43.

<sup>3</sup> Münch. med. Woch., May 27 and June 3, 1913, vol. ix, Nos. 21 and 22.

no treatment the lymphocytosis usually persisted unmodified during months. This high lymphocytosis occurred almost exclusively in patients with diabetes, obesity, exophthalmic goitre, neuropathies, asthenia, or various neuroses. Analysis of the cases demonstrated that the lymphocytosis is a manifestation of functional disturbance in the lymphatic system, chiefly of the thymus and the ductless glands. His research indicates further that asthenia and other affections of the nervous system are directly traceable to the lymphatic constitution or the status thymicolymphaticus with involvement of the glands with an internal secretion. There seems to be an inherited constitutional inferiority on the part of the glands with an internal secretion. This conception throws light on the connection between the various diatheses. He remarks, in conclusion, that the favorable action of arsenic in many neuropathic conditions is due to its influence on the lymphatic system, combating the neutrophile leukopenias and the lymphocytosis. One argument in favor of this view is the inefficacy of iron in the so-called pseudo-anemia of the neuropathic, in which arsenic is often surprisingly successful. The lymphocytosis persists unmodified by the iron, while, under arsenic, conditions return to approximately normal. This revolutionary conception that neuropathic conditions are not the result of a primary affection of the nervous system, but rather of the lymphatic system, would bring a revolution in treatment, as our measures henceforth would be directed against the abnormal functioning of the glands with an internal secretion and the lymphatic system in general.

Mehrtens<sup>1</sup> calls attention to the frequency of low polymorphonuclear leukocytic with high lymphocytic differential counts. He carefully examined the blood of 100 normal individuals, and found the average percentage of polymorphoneutrophiles in this series to be 56.55 per cent., while the lymphocytes were 37.45 per cent. The leukocytic count was made in but 20 of these cases, and averaged 7000. After a study of the literature, the author believes that his results may have been influenced by climate and geographical location, previous tuberculous infections, auto-intoxication, and the fact that the number of individuals examined was hardly large enough to eliminate chance. To get an idea of the range of the differential counts as they ordinarily present themselves in adults, the results of 500 counts were analyzed. These were taken from the various services in the Lane Hospital, and only those counts were included in which the total leukocyte count was 10,000 or below. 87 per cent. of these counts showed less than 70 per cent. of polymorphonuclear neutrophiles; 69 per cent. showed less than 65 per cent. of polymorphonuclear neutrophiles; 40 per cent. showed less than 60 per cent.; 30 showed less than 55 per cent.; 15 showed less than 50 per cent., and 2 showed less than 45 per cent.

<sup>1</sup> Archives of Internal Medicine, August 15, 1913.

The author concludes, from his work and the literature, that low polymorphonuclear differential counts are very frequently observed in clinical work. Whether this be due to climate or geographical location, previous disease, condition of metabolism, or a combination of these factors, is not clear. At any rate, it is of importance for the clinician to remember the existence of this condition when he is tempted to give undue significance to a high lymphocytic count.

**Bone Marrow.** Foot<sup>1</sup> has cultivated chicken-bone marrow *in vitro* and studied its bearing on hematogenesis in adult life. In the cultures, he has been able to trace the development of the cells through the following forms in the order given: Microlymphocyte; macrolymphocyte; large mononuclear form, myelocyte; transitional or horseshoe-nucleus form; polymorphonuclear leukocyte, and, finally, by a rounding off and dechromatization of the nucleus coincident with a rarefaction and change in the staining properties of the cytoplasm, the cell culture type. He does not claim that every microlymphocyte undergoes the complete transformation in the manner indicated. He believes merely that this line may be gone through by any microlymphocyte, and that each cell in this order has the potentiality of so doing. It often occurs that this line of development is interrupted by various digressions, or that a given cell may undergo only a part of the complete transformation; for instance, many lymphocytes go over directly into the cell culture type without undergoing the intermediate steps already indicated. The complete line given represents the usual, but not the invariable, type. The author's conclusions are that the development of the polymorphonuclear leukocyte from a mesenchymal lymphoid type of cell is possible in adult life and *in vitro* in chicken-bone marrow. These cells are rapidly proliferated by means of amitotic division of an unripe form very similar to, but smaller than, themselves. All the cells of chicken-bone marrow can undergo a transformation to a type of cell resembling, although not proved to be identical with, the cell of connective tissue.

Hedinger<sup>2</sup> has examined over a thousand cadavers to determine the distribution of the red marrow in the bones, especially in the femur, and has recorded data in 500 cases, including 44 cases of sudden death from suicide or accident. His findings are not in accord with the statements found in the text-books. In the series of 44 cases of sudden death, 11 showed fatty marrow in the femur, while 33 showed red marrow distributed more or less extensively through the femur. Of the 11 showing fatty marrow, 4 had passed middle age.

**The Spleen.** The amount of work on the spleen appearing in the literature of the past year has been comparatively large. The splenic anemias have received considerable attention, and there have been a

<sup>1</sup> Journal of Experimental Medicine, January, 1913, vol. xvii, No. 1.

<sup>2</sup> Berl. klin. Woch., November 17, 1913, vol. i, No. 46.

number of reports on splenomegaly of the Gaucher type. The preponderating amount of this work, however, has been on the subject of the spleen in its relation to hemolysis; and hemolytic jaundice, which in the past has been dealt with sparingly in the literature, this year looms as a large subject.

PRIMARY SPLENOMEGALY (Gaucher type). Wilson,<sup>1</sup> in a pathologic study of the spleens removed at the Mayo Clinic since 1904, divides the group of splenic anemias into three histopathologic classes: (*a*) Chronic lymphocytic hyperplasia; (*b*) primary proliferation of the endothelium of the spleen (Gaucher type), (*c*) primary (chronic) diffuse hyperplasia of the spleen (chronic splenitis).

From what we know of hyperplasia of other organs, the author thinks it unnecessary to assume hypothetically the presence of three different causes for the production of the three primary histological types of splenic anemia. The histopathologic picture in all three types of spleen from cases of primary splenic anemia seem to be in complete harmony with the hypothesis of the presence of a slowly acting local toxin. There are certainly spleens from clinically doubtful cases of splenic anemia which the pathologist cannot distinguish from the spleens of clinically undoubted cases; yet it must be conceded that the finding of a great hyperplasia of one or all of the tissue elements of the spleen, without other diagnostic lesions elsewhere in the body, is strong corroborative evidence of the clinical diagnosis of splenic anemia.

Wilson, in his classification, looks upon three of the cases as of the Gaucher type. He considers the process in this type to be a primary endothelial proliferation with a secondary proliferation of fibrous connective tissue, and, ultimately, a degeneration of the endothelium with contraction of the connective tissue. He believes that the large cells are much more likely to have arisen from the endothelium than from the reticulum.

A case of this disease reported by Mendlebaum, in 1912, was discussed rather fully, especially from the pathologic stand-point, in these pages last year.

Brill and Mandlebaum<sup>2</sup> give a very full description and discussion of large-celled splenomegaly which they believe should be called Gaucher's disease. Owing to the haze which surrounds the conception of medical men in reference to the Gaucher type of primary splenomegaly the authors feel prompted to make an attempt to show that this specific form of disease has little in common with the promiscuous group of diseases whose chief characteristic is an enlargement of the spleen. They believe the subject has been still further confused by the article of Wilson, referred to above, wherein he reports three cases of the Gaucher type for which splenectomy had been performed at St. Mary's

<sup>1</sup> Surgery, Gynecology, and Obstetrics, March, 1913.

<sup>2</sup> American Journal of Medical Sciences, December, 1913.

Hospital, Rochester, Minn. In a footnote to their article, they say that an examination of the slides, which were kindly sent to them by Dr. Wilson, revealed the undisputed existence of the disease in only 1 of his 3 cases. This conclusion was arrived at after careful and critical study. Later, with the permission of Wilson, these slides were submitted to Marchand for an opinion. He wrote that the first case was one of the Gaucher type, but that the other two were not. The author's define Gaucher's disease as one, the characteristic features of which are its incidence in childhood, its frequent presence in other members of the family of the same generation, a progressive increase in the size of the spleen which often reaches colossal dimensions, followed by a similar huge enlargement of the liver, a characteristic, brownish-yellow discoloration of the skin, usually restricted to the face, neck, and hands, a peculiar yellowish, wedge-shaped thickening of the conjunctivæ commonly seen on both sides of the cornea, and the prolonged and chronic course of the disease, which does not materially disturb the health of the individual. After the disease has been present for a considerable time, there is a definite tendency to hemorrhages, especially appearing as epistaxis, bleeding from the gums, and ecchymoses in the skin following the slightest trauma. The positive finding in the blood, even in the early stage of the disease, is a definite leukopenia. The erythrocytes, however, show no definite change, either in number, form, size, or hemoglobin-content until the disease has existed for a long time, when an anemia of the chlorotic type makes its appearance. The anemia is rarely pronounced at any stage. The disease is not accompanied by palpable enlargements of the superficial lymph nodes. There is no jaundice, and ascites is exceptional. The disease has none of the characteristics of malignancy, and usually is terminated by some intercurrent affection.

The pathologic feature of the disease is the presence in the spleen, liver, lymph nodes, and bone marrow of distinctive large cells, with characteristic cytoplasm and small nuclei. The enlargement of the spleen and liver is due to the presence of these cells in enormous number. In well-established cases all of these organs contain pigment giving the reaction for iron. Whereas the nature and origin of these cells are still mooted questions, the histological picture is uniformly characteristic and pertains to no other form of disease.

While there are no individual symptoms which are pathognomonic of this disease, the authors believe that a definite association of certain symptoms is sufficient to enable one to clinically diagnose its presence. It was this association of symptoms which enabled one of the authors to make the diagnosis clinically in two cases, which was subsequently confirmed by pathological examination.

The cases so far established according to their views are: (1) Gaucher, 1882; (2) Collier, 1895; (3) Picou and Ramond, 1896; (4) Bovaird,

1900; (5) Brill, Mandlebaum and Libman, 1904; (6) Schlagenhaufner, 1907; (7) von Herczel, 1907; (8) Marchand, 1907; (9) Brill, Mandlebaum and Libman, 1909; (10) De Jong and van Heukelom, 1910; (11) Mandlebaum, 1912; (12) Wilson, 1913; (13) Downes, 1913; (14) Erdmann.

Downes<sup>1</sup> case referred to, occurred in a female, aged twenty-eight years, and is the second case (Erdmann's being the first but not yet reported) in which splenectomy has been successfully carried out in America, and brings the total number of operated cases up to seven.

**Banti's Disease.** D'Espine<sup>2</sup> discusses this type of splenomegaly in children, and reports two cases occurring in infants, with the autopsy findings. The author is of the opinion that there is an unmistakable connection between splenomegaly and rachitis. Many cases of rachitic splenomegaly which are assumed to be of syphilitic origin are probably incomplete forms of Banti's disease. Inoculation of spleen tissue into animals in D'Espine's cases gave negative results, tending to confirm the assumption that the disease is not of infectious origin. Banti has recently called attention to the similarity, if not identity, between the cases of hyperplasia and diffuse fibrosis of the spleen of non-parasitic origin and the cases of true Banti's disease. Sasuchin always found the degree of enlargement of the spleen proportional to the severity of the rachitic lesions. D'Espine believes that the only pathognomonic sign of Banti's disease is the resulting cure of the anemia and cachexia through removal of the spleen.

Wolff has also reported a case of this disease in a rachitic infant, which brings the number of cases occurring in children up to 19. In 8 cases, the symptoms were merely enlargement of the spleen with anemia—the first stage. In 7 cases, hemorrhages occurred, especially in the stomach and intestines, and associated with these were urobilinuria, slight jaundice, and ascites; 4 of the cases had progressed to definite cirrhosis. In 5 of these cases taken from the literature, the first symptoms were noticed at the age of five. Splenectomy was performed in 8 of the cases, followed by recovery in all but one of the children, and among these were three children suffering from an advanced stage of the disease. Splenectomy was supplemented by omentopexy in one of the older children, and, although there existed considerable atrophy of the liver, the patient recovered. In 2 of these cases, the patients recovered spontaneously.

Gützner<sup>3</sup> reports a case of splenomegaly with anemia in a girl aged ten years, who had been under treatment for helminthiasis when the spleen began to enlarge and signs of a hemorrhagic diathesis, followed with progressive anemia, threatening to prove fatal, unless something could

<sup>1</sup> Medical Record, April 19, 1913.

<sup>2</sup> Revue Médicale de la Suisse Romande, May, 1913, vol. xxxiii, No. 5.

<sup>3</sup> Beiträge zur klin. Chirurgie, 1913, vol. lxxxv, No. 1.

be done to arrest it. This patient had suffered from rachitis. The signs and symptoms suggested Banti's disease, but had not progressed to the stage of cirrhosis of the liver and ascites. Splenectomy was performed, and, in five days following the operation, the red cells had doubled in number and soon reached their normal figure. A normal blood picture has persisted throughout the past year.

Lacoutre, Duperie and Charbonnel<sup>1</sup> performed splenectomy in a case of Banti's disease, with a fatal result, the patient dying on the twenty-seventh day after operation, apparently, from the result of an infectious process, possibly set up by emboli from the drained focus. The patient was a woman, aged thirty-nine years, whose spleen had been enlarged for seven or eight years. She showed a progressive anemia, but no jaundice. There was ascites, but no hemorrhages from congestion of the portal system, no enlargement of the lymph nodes, and no history of alcoholism, syphilis, tuberculosis, or malaria. Urobilinuria was present. The blood was of the chloro-anemic type, with 30 per cent. of hemoglobin, and there was nothing to show abnormal hemolysis. The fatal issue of this case the authors account for by the greatly depleted state of the system, the patient lacking the normal leukocytic defence to oppose effectual resistance to the affection. Of 57 cases of splenectomy for Banti's disease reported since 1909, this makes the tenth which has succumbed after operation, placing the mortality at 19 per cent. This is the same figure recorded for 61 cases occurring during the nine preceding years. The authors believe that this high mortality shows that, as the technique has improved, the splenectomy has been performed in more advanced cases. They suggest that it would be better to reserve splenectomy for the first and second stages of the disease, and not attempt such a serious operation when the cases are so advanced. When done at the proper time, removal of the spleen permits prompt and practically complete restoration to health.

**Hemolytic Jaundice.** EXPERIMENTAL. During the past year this field has been very fruitful in research. While many definite facts have been gleaned, there exists considerable confusion in correlating them, and, at times, the facts themselves appear to be contradictory.

The view that bile pigments are derived solely from the hemoglobin of blood corpuscles, and that this change, under physiological conditions, is brought about only in the liver is generally accepted at present. The work of Whipple and Hooper,<sup>2</sup> would seem to give rise to doubts as to whether the mechanism of blood-pigment formation can be explained in this simple manner. The results of the authors' experiments showed that normal and Eck-fistula dogs react in a similar manner to the intravenous injections of hemoglobin obtained from laked red cells of the

<sup>1</sup> Jour. de Méd. de Bordeaux, December 14, 1913.

<sup>2</sup> Journal of Experimental Medicine, June, 1912.

same animal. Hemoglobin appears in the urine after a few minutes, and bile pigments in one to one and one-half hours. In this simple type of hematogenous jaundice, the reaction is in no way influenced by shutting out the portal blood from the liver and cutting down its blood supply to about 25 per cent. of normal. In a second type of hematogenous jaundice produced by chloroform anesthesia, which produces central liver necrosis, there is no essential difference between the normal and Eck-fistula dog. The Eck-fistula dog, as a rule, is more resistant to this poison, but, given a definite liver necrosis, the jaundice developing will reach its maximum on the second day as in the normal animal. The jaundice must be explained in part by capillary biliary obstruction, but in part by a hemolysin formed in the injured liver cells (Joannovics and Pick).

Simple obstruction of the common duct, when combined with an Eck-fistula, gives rise to a definite low grade icterus, with bile pigment constantly present in the urine. Under these conditions, after double ligating and cutting the common duct with separation of the cut ends, the lumen of the duct may be established and bile may enter the intestine by means of a fistulous tract between the cut ends of the bile duct. The formation of bile and bile pigments is much less in an Eck-fistula dog than in a normal animal, and, consequently, the icterus is much less intense. This is probably due to a lessened activity of the liver cells because of decreased blood-supply. This observation does not harmonize with the current view that bile pigments are formed solely from hemoglobin, as there is no evidence of more hemolysis in a normal than in an Eck-fistula dog. This suggests to the authors that the bile pigment may be formed in part, at least, from other substances than hemoglobin, and, further, that bile pigment formation normally may depend in part on the functional activity of the liver cell rather than on the amount of hemoglobin supplied to it.

In a further series of experiments by the same authors,<sup>1</sup> evidence is submitted that hemoglobin can be transformed into bile pigment in the circulation when the liver has been excluded from participation in the reaction. The intravenous injection of red cells obtained from the same animal, and laked by distilled water, is similar to certain types of hemolysis which result in hematogenous jaundice. This procedure cannot be criticised on the grounds of introducing toxic substances. The hemoglobin circulating in the blood stream is rapidly changed, in part at least, to bile pigment. The change goes on with practically the same rapidity in a normal circulation, in an Eck-fistula animal, and in a dog with Eck-fistula and hepatic artery ligation. Moreover, the bile-pigment formation goes on in a dog whose liver, spleen, and intestines have been shut out of the circulation, and in

<sup>1</sup> Journal of Experimental Medicine, June, 1913.

those with a head and thorax circulation. In the last experiments, there had been no operative manipulation of the liver, and the bile pigment could not have escaped from the liver and have been absorbed by the circulation above the diaphragm: for example, by the thoracic duct. It is possible that the endothelium of the bloodvessels is the agent which brings about the rapid change of hemoglobin free in the plasma.

The authors conclude that in dogs, at least, hemoglobin can be rapidly changed into bile pigment in the circulating blood without participation of the liver.

Pilcher<sup>1</sup> has investigated the *influence of lipoids on hemolysis*. While working with a number of laking or hemolytic agents, he observed that a number of bland oils increase the hemolytic power of certain substances which are either lipoid solvents (alcohol and ether) or are soluble in oils (chloral hydrate). This holds true whether the blood corpuscles are first shaken with the oils and are then added to the plain hemolytic agent, or whether plain or "oiled" corpuscles are added to the hemolytic agent saturated with the oils. The increased hemolysis caused by the oils was not due to free fatty acids, for the oils were neutral, or at least very faintly acid, to alcohol-moistened litmus. The "oiled" blood, on staining, did not lake before the plain blood. Shaken plain blood behaved as unshaken blood. It is suggested that the oils increase the permeability of the lipoid (lecithincholesterin) cell envelope to the laking agents.

Several series of experiments were made, using 50 per cent. alcohol in normal saline as a laking agent. 5 c.c. of a 5 per cent. mixture of sheeps' corpuscles, both plain and "oiled," were added to 3.7 c.c. of plain alcohol made up to 5 c.c. with normal saline solution. The linseed and olive oil corpuscles were laked within five minutes, the petrolatum in thirty, and the plain corpuscles in sixty minutes. With 3.5 c.c. of alcohol, plain and petrolatum corpuscles were laked in about three hours, the cottonseed oil corpuscles in one and one-half hours, while the linseed and olive oil corpuscles were still laked in five minutes. In other experiments, petrolatum corpuscles were laked somewhat more readily than plain. When the alcohol was saturated with the oils, it was found that laking occurred more rapidly than with plain alcohol, so that in this series smaller quantities of alcohol were used. 2 c.c. of alcohol saturated with linseed and olive oils laked linseed and olive oil corpuscles within one hour, and cottonseed corpuscles somewhat less rapidly; the plain and petrolatum corpuscles were laked over night. Alcohol saturated with cottonseed oil and petrolatum liquid, laked linseed, olive, and cottonseed (the latter only partially) corpuscles overnight, but not plain and petrolatum corpuscles; so that linseed and

<sup>1</sup> Cleveland Medical Journal, March, 1913.

olive oils increase alcohol laking more than cottonseed oil and petrolatum. Linseed oil is soluble in ten parts of absolute alcohol, olive oil sparingly, cottonseed oil and petrolatum very sparingly. This difference in solubility may explain the greater action of the linseed and olive oils, although there was not a great difference between the action of the two, and linseed oil is much more soluble in alcohol than is olive oil. In the presence of oils even completely laked mixtures may be cloudy, so that the microscope was employed to determine when the corpuscles were in complete solution.

In a study of the *hemolytic properties of fatty acids* and the relation to causation of toxic hemolysis and pernicious anemia, McPhedran<sup>1</sup> concludes that the idea that toxic hemolysis, in disease, in poisoning by phosphorus or toluin diamine, results from the liberation of specially hemolytic fatty acids from the fatty complexes of disintegrating cells is not well supported by evidence; none of the fatty acids, still less any of the fatty complexes from which these acids can be obtained in any of the organs examined, either in this work or the work of others that has preceded it, show, on analysis, any evidence for the existence of fatty acids more toxic than the common oleic acid which is constantly being set free by hydrolysis from common fat in health.

In a paper on the *course of destruction of the blood in pyrodin anemia*, Hess and Müller<sup>2</sup> state that, in this experimental anemia, they have found by special staining methods, a substance in many of the red corpuscles which they view as a lipoid. Blood taken from the splenic artery is rich in cells with these lipoid inclusions, while the blood on its exit from the spleen is found to be poor in cells of this character. The lipoid substance has evidently been extracted and these cells can be readily differentiated from the other red cells. The blood obtained from the portal vein at its entrance into the liver is rich in cells from which the lipoid has been extracted, but, on its exit from the liver, the blood shows a poverty of these cells which the authors believe are destroyed in the liver.

During the past two years, Pearce has been investigating the relation of the spleen to blood destruction and regeneration and to hemolytic jaundice, and, up to the present, eight papers have appeared from his laboratory on the various aspects of this subject.<sup>3</sup>

Musser, Jr., and Krumbhaar<sup>4</sup> report on the *blood picture at various periods after splenectomy*. They have found that anemia usually develops quickly, and reaches its height in from three to six weeks after splenectomy has been performed. Then, with gradual improve-

<sup>1</sup> Journal of Experimental Medicine, November, 1913.

<sup>2</sup> Wien. klin. Woch., November 6, 1913.

<sup>3</sup> See PROGRESSIVE MEDICINE, June, 1913, p. 354.

<sup>4</sup> Journal of Experimental Medicine, November, 1913.

ment, the blood picture approaches the normal after about three to four months, with a complete return to normal in from five to ten months. Along with this occurs a marked leukocytosis which reaches its height in twenty-four hours, but persists to a slight degree for several months. Variations from this course, however, may occur, in that the anemia may develop slowly and be of slight degree, or the reparative process may be delayed, and, up to ten months, incomplete. The anemia, however, according to the authors, is inevitable; as is also, at a later period, some degree of repair.

Pearce and Peet<sup>1</sup> have carried out experiments to determine the effect of hemolytic serum in splenectomized dogs. They demonstrate that dogs splenectomized for one year exhibit the same increased resistance of the erythrocytes, and the same lessened tendency to hemolytic jaundice previously observed in animals splenectomized for shorter periods of time. One apparently discordant experiment suggests that possibly after a longer lapse of time than a year the lessened tendency to jaundice might not be so evident. On the other hand, it is in splenectomized animals, having the high red cell and hemoglobin content of the animal representing this experiment, that, as they have shown elsewhere, hemolytic changes may occur in equal degree to that of the control animal. They, therefore, regard the experiments here presented as in accord with those representing observations at earlier periods after splenectomy. In accord with Pepper and Peet (see section on Erythrocytes), they find that the increased resistance of the red cells after splenectomy cannot be explained by an increase in the number of reticulated cells in the circulating blood. The increased resistance of the red-blood corpuscles characteristic of the splenectomized animal is as evident one year after removal of the spleen as it is at earlier periods. So, also, is the decreased tendency to jaundice after the administration of hemolytic serum.

Krumbhaar, Musser, Jr., and Pearce<sup>2</sup> sum up briefly what their previous investigations on splenectomized dogs have led to, and say that this curious condition of anemia—that is, anemia with slow but progressive repair, increased resistance of the red corpuscles and lessened tendency to the formation of bile pigment from free hemoglobin—led them, in the hope of eliciting new facts, to the study of the course of the blood regeneration in animals receiving hemolytic agents at various periods after splenectomy. In this series of experiments, they found that in the splenectomized dog the anemia caused by hemolytic poisons (hemolytic immune serum and sodium oleate) and by bleeding, is of a severer grade, runs a longer course, and is accompanied by a less rapid regeneration of the blood than in the case of the normal dog. Also, in the splenectomized dog, especially after the use of hemolytic serum, the leukocytosis is greater than in the normal animal.

<sup>1</sup> Journal Experimental Medicine, November, 1913.    <sup>2</sup> Ibid., December, 1913.

The splenectomized dog almost uniformly exhibits an increased resistance of the red cells to hypotonic salt solution, but, after the administration of hemolytic poisons, and especially hemolytic serum, this increased resistance disappears, and a decreased resistance persists for long periods of time. The same change occurs in the normal dog, but, in the latter, the return to the previous degree of resistance is more rapid than in the splenectomized animal.

At first glance these results appear to contradict some of their earlier work, in which it was shown that the red cells of the splenectomized animal are more resistant to hemolytic agents than those of the normal dog, and that in such animals, hemolytic jaundice is not so readily produced. On the basis of these observations, concerning the accuracy of which repeated experiments have furnished a large mass of corroborative evidence, one would hardly expect a hemolytic poison to cause in the splenectomized animal a more severe anemia than that which occurs under similar circumstances in the normal animal. The present investigation, however, shows this to be the case, and, moreover, that hemolytic poisons change the more resistant cells of the splenectomized animal to less resistant cells, this diminished resistance persisting longer than in the normal dog.

It is evident, therefore, that the immediate destruction of the red cells by a hemolytic agent, as shown by hemoglobinuria and the result of the blood examination, is not the only factor in the production of the anemia, but that, in the splenectomized animal, some added factor plays an important part. The hemolytic agent inaugurates an acute anemia, but the absence of the spleen is an important secondary factor in increasing the severity of the anemia and in either prolonging its course or delaying the process of repair.

It would appear, therefore, that of the phenomena associated with the absence of the spleen, two, the increased resistance of the red cells and the decreased tendency to jaundice after the administration of hemolytic poisons, are co-related and intimately associated with the anemia of splenectomy, but that the anemia itself is dependent upon some factor as yet unknown, which operates in the absence of the spleen. This unknown factor would also operate in the anemia produced in such animals by hemolytic serum, and more especially so as the hemolytic anemia is characterized by a decreased resistance of the red cells. As the factor dependent on the absence of the spleen does not operate in the normal animal, the latter recovers quickly. It seems possible, therefore, thus to explain the more severe and more prolonged anemia in such animals, even though they may have more resistant corpuscles.

The researches of Pugliaiese and Luizzatti, quoted by Lankhout,<sup>1</sup> on the *functioning of the spleen* show that splenectomized dogs can endure

<sup>1</sup> Nederlandsch Tijdschrift voor Geneskunde, Amsterdam, Ceteler, 1913, vol. ii, No. 15.

twice the amount of pyrodin that the normal dog can stand. Pyrodin has a destructive action on the blood, but, in the splenectomized dogs, this does not go beyond a certain limit, while the destruction proceeds indefinitely in the non-operated animals. They observed that a small dose of pyrodin causes albumin, blood and bile pigments to appear in the urine, but this does not occur in the spleenless animal. They explain this difference as follows: In the non-operated animal, the blood pigment, which is formed under the influence of a hemolytic poison, is deposited in the spleen and from thence it is carried to the liver. The liver cell responds to this with increased functioning. If the spleen has been removed, the blood pigment deposits itself in the marrow, thus over a larger area; and so the pigment can only reach the liver cell by way of the general circulation, and when it arrives at the liver it is much diluted. In the splenectomized animal, it reaches the liver by the hepatic artery and in the normal animal by the portal vein.

Pribram<sup>1</sup> has reported extensive researches on dogs with the idea of studying *hemolysis resulting from congestion of the spleen*. By producing congestion in the spleen, he readily produced a urobilinuria; and, according to the author, this substance in the urine is the only sign known to date indicating abnormally increased destruction of red blood corpuscles. He failed to produce this urobilinuria by other means. Even intravenous injection of a substance known to be directly destructive to the blood did not produce it. Further experiments showed that stasis in the inferior vena cava, such as occurs with uncompensated valvular lesions, leads to urobilinuria to an intense degree. He has never encountered a clinical case of isolated stasis in the spleen with exaggerated destruction of red corpuscles and consecutive anemia and urobilinuria, but a number of such cases have been described in the literature. All the patients had varicose enlargement of the splenic vein, and its course was extremely tortuous; sometimes the vein was kinked and actual varicose tumors developed in the hilus of the spleen. The spleen was always much enlarged, but generally there were no other pathologic findings except possibly slight cirrhosis of the liver, but all the patients showed signs of abnormal destruction of blood, anemia, and urobilinuria. The most remarkable feature in the cases is that the patients are young, and the vascular apparatus elsewhere seems normal. Pribram thinks that this syndrome of varices in the splenic vein with extreme congestion in the spleen and destruction of the red cells must be regarded as a special affection *sui generis*. He regards the sclerosis and varicose enlargement of the vein as the primary trouble, and suggests that this peculiar pathologic condition of the veins in this region may be traced to an infectious process in the umbilicus in the first weeks of life. There was a history of such a process in two

<sup>1</sup> Wien. klin. Woch., October 2, 1913.

of Türek's patients. Several of the cases on record were in children. There is also the possibility of injury from toxic products formed in the intestines which are liable to act most intensely on the nearest veins; namely, the portal system.

In a voluminous article reporting extensive research and clinical experience in hemolytic infections, Banti<sup>1</sup> concludes that the agents of hemolysis can be divided into two great classes: the first being those which act directly and almost exclusively on the erythrocytes in the blood stream, with no appreciable active coöperation on the part of the organism. Distilled water belongs to this class. The other class of hemolytic agents act directly on the red cells, but have also the power of stimulating the hemolytic organs to an excessive destruction of blood corpuscles. To this class belong serums, phenylhydrazin, etc. The organs on which this class act are the spleen most of all, and then, to a far less extent, on the liver, the lymph nodes, and the bone marrow. The spleen is, above all, the most sensitive and the most active in hemolysis. In clinical hemolytic splenomegaly, four factors are at work: the agent causing hemolysis; the excessive hyperactivity of the spleen in the hemolytic process; the anemia (the consequence of the excessive hemolysis), and the (occasional) jaundice—also the consequence of the excessive hemolysis. If the hemolytic agents are sufficiently potent to induce excessive hemolysis also in the secondary hemolytic organs, either splenectomy would be useless or it would induce merely simple improvement, transient or permanent. When not so potent, splenectomy removes the principal instrument at work in the hemolytic process, its hyperfunctioning being revealed by its enlargement and by the anemia resulting from the excessive hemolysis. The splenectomy does not remove the unknown primary hemolytic agents, but it deprives them of their powerful ally, the spleen. They are then unable to do harm, and the splenectomy would thus be clinically equivalent to a complete cure. This conception of the mechanism of hemolysis throws light on other forms of anemia. It seems probable that certain forms of progressive pernicious anemia are due to some abnormal process of excessive hemolysis of splenic origin. If this proves true, it might be possible to arrest the progressive anemia by removal of the spleen, and thus bring the patient back to health.

**TYPES.** The two principal types of hemolytic jaundice, the *congenital* of Chauffard, and the *acquired* form of Widal, were described and discussed in these pages two years ago. At the present time, in the light of our knowledge of these interesting affections, a gradient series of types of hemolytic jaundice may be described which merge into pernicious anemia. These, briefly stated, are a type in which there occurs slight jaundice with no splenomegaly, no anemia, and

<sup>1</sup> Semaine Médicale, July 2, 1913.

but slight fragility of the erythrocytes. These cases are entirely benign, and run along with little or no complaint on the part of the patient. The next type is that described by Chauffard, with slight to moderate jaundice, moderate splenomegaly, moderate anemia, with fragility of the red cells. This type runs a chronic course and is not so dangerous. There are variations to less and more marked types, but these are not so pronounced as the variations in the acquired form of the disease described by Widal. The third group is the Widal, or acquired, type. Here we have more marked jaundice, marked splenomegaly, more profound anemia with fragility of the red cells. The course of this type is acute, and the prognosis is much less favorable. The variations in this type are more marked than in the Chauffard type. A fourth group resembles the Widal type, but shows little or no fragility of the erythrocytes. This type merges with certain forms of pernicious anemia which have been described.

A case of the Chauffard type is presented in full by Richards and Johnson,<sup>1</sup> with interesting comment and discussion. The patient was a female, aged twenty-three years; married; housewife; and was admitted to the hospital complaining of jaundice and a swelling in the upper left abdomen. She had been jaundiced since birth. The jaundice varied in intensity and was not accompanied by pruritus, hemorrhages, or languor. The stools were never clay colored, so far as the patient knew. The menstrual history was normal. The patient was married eighteen years and had two children; the first was stillborn; the second was premature, and did not live. At the age of six years she had a severe attack of inflammation of the joints, with fever, and pain in the region of the heart. Between the ages of one and a half and fourteen years the patient was subject, at intervals varying from a few months to a year, to attacks of abdominal pain accompanied by vomiting, fever, and a decided increase in the jaundice. At such times, the stools, so far as she knew, were normal in color. After one of these attacks, at thirteen years of age, the patient was seen by a physician who stated that at that time the jaundice was marked, there was a distinct anemia and nothing abnormal was detected on examination of the abdomen. Six months later a cholecystotomy was performed and several gallstones were removed. Following this, the patient believed that she was free from jaundice for a year and a half, after which it again returned. In 1909, after an unusually severe attack of abdominal pain with "chills and fever," her spleen was discovered to be enlarged.

Since that date the patient has had three febrile attacks, each accompanied by an exacerbation of the jaundice and a distinct sense of swelling in the upper left abdomen. These seizures have not been attended, however, by chills or abdominal pain. The stools, as in

<sup>1</sup> Journal of American Medical Association, November 1, 1913.

previous attacks, were never clay-colored. In the last attack before admission (March, 1912), fever ranged as high as 103° to 104° F., for a day or two, the jaundice was intense, and the swelling in the left abdomen (spleen) was marked.

*Physical Examination*, April 5, 1912. The patient is a well-nourished young woman remarkably free from all discomfort. The skin of the entire body and the scleræ are jaundiced a deep orange yellow. The mucous membranes are somewhat pale. The tongue is clean. Pupillary and other reflexes are active. Intelligence is keen. There is no adenopathy. The heart is 12.5 cm. in width. A soft systolic murmur, only slightly transmitted, is heard at the apex; another, louder than the first, with its maximum intensity in the first left interspace, is heard at the base. Pulse is regular, 80 to 84 per minute. Systolic blood-pressure is 116. The lungs are negative.

The spleen is greatly enlarged. The edge is readily palpable 8 cm. below the costal margin, descending on deep inspiration somewhat beyond the umbilicus. On bimanual palpation, it is freely movable, very firm, and free from tenderness.

The liver is slightly enlarged; the upper border is at fourth rib in the midclavicular line; the lower border, soft and palpable, is just below the costal margin.

*Laboratory Findings*. Urine: Usually highly colored. Traces of albumin present on several occasions. Sugar absent. No indican. Bile negative. Urobilinogen (paradimethylaminobenzaldehyd) and urobilin (Schlesinger's; spectroscopic) reactions strong. Microscopically nothing significant.

Stools: Deeply pigmented. No blood, pus, ova, or parasites. Corrosive-sublimate tests shows hydrobilirubin. No bilirubin.

Blood: Records prior to admission: March 21, 1904, red-blood corpuscles, 3,850,000; white-blood corpuscles, 13,250; hemoglobin, 47 per cent. April and May, 1912, average count red-blood cells, 2,600,000; white-blood cells, 7000 to 9000; differential, polymorphonuclear neutrophiles from 50 per cent. to 60 per cent., and lymphocytes from 30 per cent. to 40 per cent.

Observations on the blood after admission were as follows: March 20, 1913: Red-blood corpuscles, 2,600,000; hemoglobin, 45 per cent. (Fleischl-Miescher); color index, 0.87; white-blood corpuscles, 10,800. Differential count of 500 cells (Wright's stain):

|  |      |           |
|--|------|-----------|
| Polymorphonuclear neutrophiles . . . . . | 66.6 | per cent. |
| Lymphocytes . . . . .                    | 22.0 | "         |
| Large mononuclears . . . . .             | 6.2  | "         |
| Transitions . . . . .                    | 3.05 | "         |
| Eosinophiles . . . . .                   | 0.6  | "         |
| Basophiles . . . . .                     | 1.0  | "         |
| Degenerate forms . . . . .               | 0.6  | "         |

In April and June similar findings were noted, except for a greater number of leukocytes (12,000 and 12,800) and a slightly higher percentage of polymorphonuclear neutrophiles. Red cells have constantly manifested microcytosis, anisocytosis, anisochromia, and polychromatophilia. Poikilocytosis is slight. Many erythrocytes contain basophile granules; a few show Jolly-bodies. Erythroblasts are very rare. Platelet count (Wright's method), 240,000 per cubic millimeter. Coagulation time, normal.

Osmotic resistance of erythrocytes:

|   | Initial hemolysis.   | Complete hemolysis.  |
|---|----------------------|----------------------|
| March 20, 1913, whole blood . . .       | 0.72 per cent. NaCl  | 0.46 per cent. NaCl  |
| April 30, 1913, whole blood . . .       | 0.65 per cent. NaCl  | 0.40 per cent. NaCl  |
| April 30, 1913, washed corpuscles . . . | 0.675 per cent. NaCl | 0.475 per cent. NaCl |
| June 6, 1913, whole blood . . .         | 0.70 per cent. NaCl  | 0.40 per cent. NaCl  |
| June 6, 1913, washed corpuscles . . .   | 0.80 per cent. NaCl  | 0.45 per cent. NaCl  |

Blood serum: Clear, bright golden yellow, without a trace of hemoglobin. Syllaba's test (modification of Conner and Roper) shows a strong reaction for bilirubin. Urobilin not detected. Patient's washed corpuscles not agglutinated by her own serum. Freezing point of serum —.58° C. Wassermann reaction negative.

Operation: On May 18, 1912, at the patient's request, a laparotomy was performed. A much shrunken gall-bladder, not containing any calculi, was removed. The patient was discharged from the hospital June 8, 1912.

Present condition: June 6, 1913: During the past year the patient has felt remarkably well, and carries on her household duties without difficulty. She had been quite free from any of the acute attacks until recently, when she went through a rather milder one than usual. The jaundice, as hitherto, has been constant, though at times it is slightly less marked than at others. The spleen is firm and greatly enlarged, the lower edge being 12 cm. below the costal margin. The lower border of the liver is felt a trifle lower than it was a year ago, and is also slightly firmer. The patient has been kept constantly on iron, as she finds that if it is discontinued she soon begins to feel somewhat weak.

Gaisbock<sup>1</sup> reports in detail 3 cases of hemolytic jaundice of the acquired type. All 3 occurred in males. The first case began at ten years of age, the second at twenty-five years, and the third at twenty-two years. In the early years of life, in all three, there was a tendency to epistaxis, and the first case suffered from bronchial asthma. In all three, the gastro-intestinal functions were below normal. They all showed a tendency to infantilism of the heart and great vessels, while in the second case there was a persistent thymus. General enlargement

<sup>1</sup> Deut. Archiv f. klin. Med., 1913, vol. ex, p. 5 and 6.

of the lymphatic glands was noted in all three cases. In discussing the pathogenesis of the disease, the author says that this is not yet cleared up; but, in the three cases at hand, he reasons that there is a constitutional inferiority of the organism which renders it less resistant to toxic factors. Gaisböck concludes that the hemolytic anemias with increased fragility of the erythrocytes may run an acutely fatal course, as shown in this third case, and that this anemia may show the characteristic signs of an acute leukemia, as exemplified in his second case. He calls particular attention to the constitutional phenomena present in all three cases as probably being the underlying cause of the disease.

In the congenital form of hemolytic jaundice, the decreased resistance of the red cells is always demonstrable, but this phenomenon in the acquired form has proved to be variable. Sometimes in this type of the disease the lessened resistance of the erythrocytes cannot be demonstrated, unless they are separated from the plasma and washed.

Mosse<sup>1</sup> has reported 2 cases of the acquired, or Widal type, in which the resistance of the red cells was found to be normal.

**Pernicious Anemia.** The close relationship, or merging, of hemolytic jaundice on the one hand, with pernicious anemia on the other, is shown by the reports of several cases during the past year.

Antonelli<sup>2</sup> describes a case of acquired hemolytic jaundice which differs from the usual type in that its clinical course and its complicated hematological character were typical of pernicious anemia. Splenectomy in this case brought about a slow and progressive improvement, with complete disappearance of all clinical symptoms, and complete recovery of normal hematological relations. This is of importance in so far as it proves that forms of pernicious anemia can be influenced by splenectomy to the extent of complete cure. The extraordinary influence of the splenectomy proves, in this case, that the spleen is of great pathogenetic importance in the hemolytic process, if not the primary cause of the disease. The author's search for anti-iso- and hetero-hemolysins in the blood-serum and in the spleen extract, proved futile. They consider that the intra-organic destruction of blood corpuscles cannot be considered identical with the simple phenomenon of hemolysis *in vitro*.

Poynton,<sup>3</sup> on the other hand, reports a case of anemia of the pernicious type with acholuric jaundice. Here we have the history of a virulent anemia with acholuria, enlargements of the liver and spleen which varied with the course of the illness, with fever which was remarkably persistent and which varied inversely with the red cell count. The changes in the blood were extreme. The red cells were greatly diminished in number, the color index was high. There was a tendency to increase in the

<sup>1</sup> Berl. klin. Woch., 1913, No. 15.

<sup>2</sup> Policlinico, sez. med., April and May, 1913.

<sup>3</sup> Clinical Journal, London, February 5, 1913.

size of the corpuscles, and there was one definite blood crisis. The fragility, however, was not greater, but less, than normal. A considerable leukocytic increase gave way to a leukopenia. Digestive disturbances were prominent throughout, as were also mental symptoms and a diminution of reflexes. No septic focus could be found, though it is possible that such existed. It is in the face of these facts that the authors venture to compare some of the features of this case with those that occur in congenital acholuric jaundice.

In 1909, Chauffard and Vincent described a case of profound anemia in which they were able to demonstrate autohemolysins. On account of its similarity to "Ictère hémolytique," they called it, in contradistinction, "Ictère hémolysinique." Roth<sup>1</sup> reports a case of pernicious anemia with signs of extreme destruction of the erythrocytes in which he was able to demonstrate autohemolysins and auto-agglutinins. Their researches showed that it can hardly be assumed that these phenomena are due to the formation of specific autohemolysins or auto-agglutinins. Apparently, they are the result of a primary structural defect or injury of the erythrocytes, whereby they more easily bind certain iso-hemolysins and their respective agglutinins. He believes that, in the light of these findings, there is not sufficient proof to consider Chauffard's "ictère hémolysinique" as a typical and distinctive disease type.

**ETIOLOGY.** Pileher,<sup>2</sup> in an analysis of 433 cases of abdominal complaints presenting the symptoms of achlorhydria hemorrhagica gastrica, most of which were observed at the Mayo Clinic, found 34 cases of pernicious anemia. In concluding his short article, he presented the following facts for consideration: achlorhydria is merely a symptom denoting a marked degree of chronic gastritis. It is usually evoked through extra-gastric irritative factors, which are, in many instances, capable of correction. There are, without exception, present in such stomachs great numbers of bacteria ordinarily considered pathogenic, among which streptococci are especially to be noted. Practically all recorded cases of authenticated pernicious anemia present the symptom of achlorhydria, and, in his own series of 34 cases, the presence of occult blood in the stomach extract. 34 instances of pernicious anemia were noted in patients presenting the symptom of achlorhydria hemorrhagica gastrica. In a few of these cases the lack of hydrochloric acid and the presence of occult blood were known to be present at least one year before any blood changes were to be noted. In others, the phenomena of paresthesia were evidenced sometime previous to blood impairment, and many had suffered for years from chronic gastro-intestinal complaints. 80 per cent. of cases of pernicious anemia have increased temperature some time during the course of the disease.

Pure cultures of streptococci have been found by competent observers

<sup>1</sup> Deut. Archiv f. klin. Med., 1913, vol. ex, 1 and 2.

<sup>2</sup> American Journal of Medical Sciences, August, 1913.

in the blood of patients with pernicious anemia who were running a fever. Bacterial hemolysins are known to produce anemia resembling the pernicious type, as are other toxic substances, among which may be classed the lipoid group. Efforts directed to the control of bacterial growth in the body, and particularly in the gastro-intestinal tract have caused complete remissions in this disease in some instances. The phenomena of occurrence, remission, and re-occurrence of the blood picture characteristic of pernicious anemia may be explained by our present knowledge of the action of toxins from whatever source, impairing the formation of antibodies until a bacteremia is produced which may be clinically recognized. The toxins present being eliminated by the profuse flora in the gastro-intestinal tract, the impairment of bodily resistance is accomplished through their absorption and the disturbance of digestion in cases of achlorhydria.

Finally, reactive and combative ability of patients suffering with achlorhydria varies in different patients, and on this ground alone might be explained the relatively rare occurrence of pernicious anemia, although the occurrence of achlorhydria is fairly common. Thus the development of pernicious anemia would seem to be dependent on a personal idiosyncrasy of certain individuals; in fact, we must revert for the real etiologic factor of its inception to an embryonic tendency, the presence of which we are not as yet able to determine, until it has been stimulated into an active destructive agent of the blood by the toxins absorbed from the profuse bacterial flora present in the stomach.

The hemolytic nature of oleic acid being established, Adler<sup>1</sup> raises the question why we do not all die of anemia since such large quantities of triolein are taken in with our food. Triolein is split by the ferments of the digestive tract into oleic acid and glycerin. Poulain and Stheeman have shown that the lymph glands are organs for the internal digestion and assimilation of both the food and tissue fats. Adler reasons that if the lymphoid tissue acts as a regulator of the fat metabolism, then the lymphoid structure of the intestinal wall may have a similar function and may reconstruct the triglycerides from fatty acid and glycerin. Hence, it follows that if an anemia is to be brought about by the introduction of a hemolytic fat into the digestive tract, the fat must be ingested in quantities large enough to exhaust the ability of the lymphoid tissue to metabolize it, or the lymphoid tissue itself must be weakened or lessened in amount. The author undertook a number of experiments on rabbits to test this hypothesis, and arrived at the following conclusions:

Fat, in the form of olive oil or cottonseed oil is toxic to rabbits, if fed in sufficiently large quantities.

<sup>1</sup> Journal of Medical Research, May, 1913.

The toxicity of cottonseed or olive oil depends upon its content of unsaturated fatty acid.

The more unsaturated the fats fed, the greater the toxic effect.

Long continued daily feeding of non-toxic doses of oil produces blood crises resembling pernicious anemia.

Long continued feeding of oil produces extreme emaciation.

Long continued feeding with non-toxic doses of quinine protects rabbits against the effects of fat intoxication.

This protective action of quinine is probably due to an effect upon the lymphoid tissue.

The anemia thus produced is probably due to a destruction of red cells in the bloodvessels of the abdominal organs rather than to a direct effect upon the bone marrow.

This effect, being at the periphery in respect to the blood-forming organs, acts as a stimulant to the bone marrow, and, as a result, high red blood counts are encountered.

The hemolytic substance being a fat is not capable of true solution in the body fluid. It is therefore present in the body in the form of more or less finely divided colloidal particles.

The hemolytic effect is not a uniformly diffused one, but is dependent upon the meeting of a particle of hemolytic fat with a red cell.

The degree of injury to the individual cell depends upon the size and number of particles acting upon it.

The anemia is, therefore, not one uniformly affecting the red blood cells. The red cells show all possible variations from well-colored and normally formed individuals to extreme achromia, etc.

The manifestation of the toxicity of fat is due to the summation of individual reactions between body cells and effective particles.

These results seem entirely at variance with the views of McPhedran.<sup>1</sup>

Ludke and Fejes<sup>2</sup> have produced in various species of animals clinical conditions and pathological findings corresponding closely to those of pernicious anemia in the human being. They injected subcutaneously and intravenously solutions, in alcohol or ether, of the toxins of different intestinal bacteria; typhoid, typhus, dysentery, etc. These toxins were thermostatic and actively hemolytic. The virulence of the bacteria was found to be greater from diseased than from healthy intestines, and this virulence was increased by growth upon inflamed intestinal surfaces. According to their investigations, they are led to believe that cryptogenetic cases of pernicious anemia are not caused by simple gastro-intestinal auto-intoxication. The lipoids obtained from the bacteria grown on inflamed intestinal surfaces lead to further inflammatory processes in the intestinal mucous membrane. The chain of causes for the genesis of these cryptogenetic anemias is still incomplete.

<sup>1</sup> Loc. cit.

<sup>2</sup> Deut. f. Archiv. f. klin. Med., 1913, vol. ex, 5 and 6.

We do not know how the hemolyzing and anemia-producing substances are freed from the intestinal bacteria, nor how they get into the blood in order to bring about the injurious action in the bone marrow and the blood. Likewise, the significance of the more intimate processes in bothriocephalus anemia requires further investigation. The explanation of why pernicious anemia affects only certain individuals, and why chronic and intensive inflammatory processes of the intestinal tract do not generally lead to the formation and action of hemotoxic poisons, will remain difficult for a long time. We must satisfy ourselves here with the factor of predisposition to the blood disease.

Hopkins<sup>1</sup> carried out a series of experiments with the aim of ascertaining, if possible, whether extracts of stools from cases of essential progressive pernicious anemia contained hemolyzing substances not found in normal stools or in stools in other diseases. If repeatedly present this could be regarded as of some use as a further step in the clinical diagnosis of a disease the etiology of which is still uncertain, and the classification of which is hardly satisfactory. The results were so inconstant in this series of cases that the author felt that no dependence could be placed on this test, either as an aid to clinical diagnosis or as a means of enlightenment etiologically.

In order to test Berger's statement that a lipoid hemolytic substance present in the intestinal walls is the cause of pernicious anemia, Ewald and Friedberger<sup>2</sup> tested the hemolytic action of an emulsion of the tissues of the intestinal walls from two recent cases of fatal pernicious anemia. They were unable to detect any hemolytic action whatever on the part of the emulsion and, hence, failed to confirm Berger's statement.

**PATHOLOGY.** Nieol<sup>3</sup> has studied a case of pernicious anemia occurring in a woman, aged forty years, who died of profuse epistaxis. Post-mortem examination revealed a high-grade anemia of all the organs, red bone marrow in the long bones, a hemosiderosis of the liver and kidneys, and a marked fatty degeneration of the heart muscle. In addition to the blood found in the nares, an enormous amount of blood was found in the stomach, and old blood was found in the intestines. There was enlargement of the retroperitoneal glands, splenic tumor, and edema of the lungs. Microscopically, the bone marrow showed the picture of pernicious anemia. In addition to typical myeloblasts and myelocytes, numerous nucleated erythrocytes were found. In the spleen, blood formation was not apparent. Erythroblasts, myeloblasts, and myelocytes were not present, and the hemosiderin reaction was negative. The retroperitoneal lymphatics microscopically showed a large cell growth. These large cells occurred singly and in masses. They were

<sup>1</sup> Archives of Internal Medicine, March 15, 1913.

<sup>2</sup> Deut. med. Woch., July 3, 1913.

<sup>3</sup> Deut. Archiv f. klin. Med., 1913, vol. exi, 5 and 6.

stained by different methods, and tested by the oxydase reaction. In concluding, the author says that, in this case, there is found a diffuse growth of cells similar to myeloblasts in the lymph glands. These are in part true myeloblasts, and in part pathological myeloblastic forms or forerunners of myeloblasts. All of these cells give a positive oxydase reaction, and, hence, according to the author, cannot be lymphoblastic plasma, cells, Goldman's "pyrrol" cells, sinus endothelial cells, or fetal tonsil cells.

This case of pernicious anemia with a myeloblastic growth in the retroperitoneal lymphatics suggests the question proposed by Ellermann, whether or not pernicious anemia is a systemic disease, and that leukemia and pernicious anemia are merely different forms of one and the same process (see PROGRESSIVE MEDICINE, June, 1913, p. 304).

The rarity of family pernicious anemia is referred to by Bartlett<sup>1</sup> who reports four cases of this disease occurring in the same family. He refers to the reports of this condition by Sinkler and Eshner, Klein, Cabot, Weil and Gilbert and Patek (see PROGRESSIVE MEDICINE, June, 1912, p. 278). He describes the four cases and remarks that in this family of eight, within a period of thirty years, four deaths have occurred, two of them definitely due to pernicious anemia, and the other two, judging by the most evident symptoms and the autopsy findings, were also due to this disease. Another case of marked, prolonged anemia of either the chlorotic or secondary type occurred in a daughter of this household. All five patients lived either on the home farm, which was in northern Vermont, or, in one case, a short distance from this, nearly all their lives. A thorough search for parasites proved negative. The water supply, which was suspicious, was carried through an iron pipe from a spring situated 60 rods away, only a short distance from the buildings on a neighboring farm, and on a lower level than the stables and yards of this farm. This same supply, however, has been used for many years for two other families living in the buildings just mentioned, and without evidence of injurious results. In all of these cases there was distinct evidence of disturbance in the digestive tract. Most of the patients complained of continued sore mouth and tongue, and each had repeated attacks of bilious vomiting. They were of the opinion that these attacks came on more often in the spring; and, since that is the season in which maple sugar is made and eaten in large amounts, they were inclined to attribute these symptoms in some way to the eating of the sugar. In conversation with physicians of this region, Bartlett found that, for some reason, this territory has more unexplained anemia than they see elsewhere, this including the anemia of young women. The author received the impression that there is ground for the belief of these physicians that, for some reason, there is,

<sup>1</sup> Journal of American Medical Association, January 18, 1913.

in this particular region, an unusual amount of severe anemia, the cause of which offers an interesting problem for solution.

**SYMPTOMS.** Riggs<sup>1</sup> describes and discusses five cases of pernicious anemia associated with marked nervous phenomena. He calls attention to the fact that these nervous symptoms, usually of degenerative changes in the cord, may long precede the incidence of the anemia. These symptoms may be purely subjective, such as numbness in the arms and legs. One patient complained that the bones were going through the flesh. Paresthesias are strikingly noticeable. The knee-jerks may be normal, absent, or exaggerated. Ankle clonus and the Babinski reflex may, or may not, be present. Paraplegia may be partial, so that the patient may move the legs freely in bed, or it may be complete. Usually associated with this there is loss of control over the bladder and rectum. Lightning pains and objective sensory disturbances are common. Wilson recently reported a case in which gastric crises were present. Dissociation, as in syringomyelia, has been observed. Dimness of vision is quite frequent and occurs early. Optic neuritis, optic atrophy, and hemorrhages associated with retinitis are occasionally seen. Mentality is, as a rule, unimpaired, although psychotic symptoms have been reported. Camp (see PROGRESSIVE MEDICINE, June, 1913, p. 308) and others have described cases in which the mental symptoms and signs of paresis were clearly marked.

Stern<sup>2</sup> believes that without question periodical soreness of the tongue, gums, and palate is the most reliable of the inaugural symptoms of pernicious anemia, and that for some time this symptom has been known to occur in the course of the affection at a stage when its clinical and hematologic picture is fully developed. The author has observed this symptom in the initial stages in two cases of genuine pernicious anemia, one of which has since terminated fatally. It is present in another apparent case of the affection still under observation in which, however, the blood picture is not absolutely characteristic (see PROGRESSIVE MEDICINE, June, 1913, p. 307, and June, 1911, p. 260).

**PROGNOSIS.** Schüpbach<sup>3</sup> declares that the prognosis of pernicious anemia developing during pregnancy or the puerperium differs from that of pernicious anemia in general, as recovery is possible under arsenic and evacuation of the uterus, spontaneous or induced. Nägeli has reported complete recovery for eleven years to date in 2 cases, and for five years in another case. Two of his patients bore other children later with no return of the anemia. The results of recent research suggest that the anemia is due to deficient production of antihemolysins; this assumption is confirmed by the fact that the fetus never seems to suffer from the anemia. The mortality is high among the children,

<sup>1</sup> Journal of American Medical Association, August 16, 1913.

<sup>2</sup> Archives of Diagnosis, New York, October, 1913.

<sup>3</sup> Correspondenz-Blatt f. Schweizer Aerzte, vol. xlivi, Nos. 45 and 47.

simply because the anemia brings premature delivery. Schüpbach reports 2 cases, one in a woman aged twenty-five years, pregnant for the fourth time. During her last pregnancy, she had had transient nephritis, and the symptoms of the pernicious anemia were ascribed to recurring nephritis at first, and thus time was wasted before premature delivery was induced; it was then too late to save her. The fetus was well-developed; the blood supply was good, both in quality and quantity. Schüpbach knows of no other published report in regard to the findings in the fetus of a mother dying of pernicious anemia. Her sister had died a few years before from pernicious anemia. The second patient also succumbed not long after delivery induced at the eighth month. She had passed through eight pregnancies in eight years, with nine children, and was too weak to rally.

HEMOLYTIC CONDITIONS. TREATMENT. *Splenectomy*, which has been advocated and carried out as a successful measure in the treatment of primary splenomegaly of both the Banti and Gouger type, is advised, and has been successfully used in the treatment of the various types of *hemolytic icterus*; and some authors of the year go so far as to advise resort to this measure in the treatment of at least some forms of pernicious anemia. Kahn presented before the German Congress for Internal Medicine, in session at Wiesbaden in April, 1913, a series of cases of so-called hemolytic icterus in which splenectomy had been performed. All of these cases were characteristic. Seven were of the congenital, or familial, type, and three of the acquired variety. In two of the patients, the operation was followed by very rapid improvement; the jaundice disappeared, and the condition of the blood rapidly approximated normal. Immediately after operation, there was a pronounced excretion of bile pigment in the urine, which was not present before operation. After this temporary increase of biliary pigment, the urine became entirely free from it. In a like manner, the nitrogen and uric acid contents of the urine, after a temporary increase, showed a return to the normal. The red-blood corpuscles acquired a marked increase in resistance. Kahn infers from this that the spleen is not only secondarily involved in the disease, but that it is the primary seat of the affection. In the discussion of Kahn's paper, Decatello, of Vienna, referred to a case of the borderline type between hemolytic jaundice and pernicious anemia in which there was distinct fragility of the red cells. In this case, splenectomy was followed by excellent results.

Eppinger<sup>1</sup> concludes, from his experience with splenectomy in 10 cases, that it is liable to have a curative action whenever there is destruction of the blood from any cause. Not only in hemolytic jaundice but also in pernicious anemia, benefit may be derived from splenectomy. He performed the operation in 2 cases of hemolytic jaundice; in two of

<sup>1</sup> Berl. klin. Woch., August 25, 1913, vol. i, No. 34.

pernicious anemia; in three of Banti's disease; in two of cirrhosis of the liver; and in one of severe catarrhal jaundice threatening transition into acute yellow atrophy of the liver. The result, in the hemolytic jaundice and pernicious anemia cases, was surprisingly good; the urobilin in the stool dropped from 3.95 before to 0.62 a week later in one of the former cases, and from 0.65 to mere traces in one of the pernicious anemia cases, while the reds increased from 1,160,000 to 4,900,000 in six weeks, and the weight increased by 8.8 pounds. The spleen was not enlarged in either of the pernicious anemia cases. During the five or six months since, the men have continued to gain in weight and feel perfectly well. Eppinger adds a warning that, with an apparently harmless catarrhal jaundice connected with some gastro-intestinal intoxication, the spleen may become enlarged and the temperature may rise, but contrary to ordinary catarrhal jaundice, the stools are not clay-colored. There are large proportions of urobilin and urobilinogen in the urine, and the patients are liable to succumb suddenly with symptoms of acute yellow atrophy. He has recently lost two patients under these circumstances. In a more recent case, the trouble had lasted for two months, with headache and vomiting along with the jaundice. Two days after splenectomy the urine was free from urobilin, the jaundice promptly subsided, and the patient seemed restored to complete health.

Klemperer and Hirschfeld<sup>1</sup> report two cases of pernicious anemia in which they removed the spleen, and marked improvement followed. This brings to six the total number of cases on record in which splenectomy has been done in the treatment of pernicious anemia. They based the procedure on the fact that a previous patient with Banti's disease, severe anemia with splenomegaly, developed pronounced polycythemia in a year and a half after splenectomy. The reds then numbered seven and eight millions, with hemoglobin over 120 per cent. There are also a number of other cases on record in which polycythemia followed splenectomy done for rupture of the spleen.

It is possible that the splenectomy acts better when the pernicious anemia is of recent date. In the two cases here reported, the blood picture changed at once, showing an essential influence on the regeneration of the bone marrow. No such powerful reaction on the part of bone marrow has ever been obtained by any other measure applied in treatment of pernicious anemia. The hope that the splenectomy would stimulate the production of red-blood corpuscles was fully realized, although the blood still has certain features of pernicious anemia, especially the presence of numerous megalocytes. The most interesting point in the case histories is the immediate flooding of the blood, after the splenectomy, with nucleated reds, a blood crisis of an intensity

<sup>1</sup> Therapie der Gegenwart, September, 1913.

never before observed. Time alone will show whether the benefit is durable. The greatest improvement, both subjectively and objectively, was in the ease of a tuberculous woman of thirty-six; the hemoglobin content rose from 30 to 55 per cent. in one month, and to 80 per cent. by the second month.

Huber<sup>1</sup> reports a successful splenectomy for pernicious anemia. The patient was a woman, aged thirty-four years, with a history of well-treated syphilis four years before. The pernicious anemia was in a threatening stage, hemoglobin 15 per cent., and only slight benefit was realized from repeated intragluteal injection of 30 to 25 c.c. of defibrinated blood. The splenectomy took only twenty minutes. In future he will ligate the different arteries preliminary to removing the spleen, as this would save a lot of blood. Fully 150 c.c. of blood flowed from the spleen after its removal. The patient felt better by evening, and the improvement was pronounced the next day and later. By the fifth week the hemoglobin was 50 per cent., and the reds numbered two and a half millions. There was no further edema, jaundice, or urobilinuria. The fourth week the progress toward recovery seemed to stop, and the hemoglobin dropped to 42, but increased to 43 under repeated injections of blood. The patient is now taking fresh beef spleen. She is up and about and cheerful, in marked contrast to her desperate condition before the splenectomy. The remarkable improvement that followed splenectomy in this case suggests that the spleen must be a much more important factor in pernicious anemia than has hitherto been suspected. It seems to acquire a very destructive action on the red-blood corpuscles while at the same time exerting an influence on the bone marrow, checking the production of new red corpuscles. This pathologic disturbance in the functioning of the spleen is evidently the result of the myeloid changes in the spleen which have hitherto been comparatively disregarded. Removal of the spleen, therefore, does not remove the cause of the disease, but it does away with the source of several of the most serious elements in the disease. The bone marrow may recuperate completely in mild cases when this disturbing element drops out, and, even if it is unable to do this, the general condition improves when the red corpuscles which are produced cease to be destroyed in such wholesale numbers when the spleen is gone.

Mosse<sup>2</sup> adds another ease in which the clinical picture of pernicious anemia was transformed by removal of the spleen. He considers this treatment applicable only in cases of pernicious anemia with much hemolysis. The extent of the blood destruction can generally be determined by testing the resisting power of the red corpuscles to salt solution and the patient's serum and alien serum. Mosse's patient was a

<sup>1</sup> Berl. klin. Woch., November 24, 1913, vol. i, p. 47.

<sup>2</sup> Ibid., November 10, 1913, vol. i, p. 45.

woman, aged thirty-eight years, and the great benefit following splenectomy has persisted unmodified to date.

Park<sup>1</sup> reports what he believes to be the first case of pernicious anemia cured in this country by the use of *thorium X*. The patient was a male, fifty years of age, and a teacher by occupation. He had yellow fever in 1888, and made a good recovery. In 1906 his health began to fail, and in 1907 his trouble was diagnosed pernicious anemia. The history of the case shows that the patient had three relapses, the last of which occurred in 1912, and in that he was treated by the author with thorium X. His condition at the time treatment was begun showed edema of all dependent parts, dyspnea on the slightest exertion, poor appetite, feeble digestion, and a blood-count of 1,200,000 red cells. In just four weeks he was about town and as vigorous as ever, with a blood-count of 4,800,000 erythrocytes. One week later the count had increased to 5,280,000.

The author quotes Bickel in the use of this treatment as administering an intravenous dose of 50,000 M units once every four days until three doses are given; and then the treatment is continued by giving a daily portion of 20,000 M units by the mouth, one-third to be taken after each meal. Park is convinced that this is the most beneficial remedy known to medical science for the treatment of pernicious anemia.

The value of *salvarsan* in the treatment of this malady is still debatable. Bramwell<sup>2</sup> reports 11 cases of undoubted pernicious anemia, with one doubtful case, which were treated with salvarsan or neosalvarsan in doses of 0.3 gram given intramuscularly. The author states that the neosalvarsan is much less irritating. In this series of cases, there resulted four apparently complete cures; 2 cases showed striking improvement; one showed considerable improvement, but ultimately developed a relapse and died. One showed slight improvement, but death intervened from bronchial pneumonia while the patient was under treatment. Two showed no improvement whatever, and one case still under treatment shows slight improvement. The author has had forty years' experience with the treatment of this disease by means of arsenic, and considers salvarsan a much superior remedy. He states, however, that further experience is necessary before one can say that the effects are permanent.

Boggs<sup>3</sup> reports 11 cases of pernicious anemia treated with salvarsan. Seven of the cases were treated in the Johns Hopkins Hospital, and in the series there were two deaths, one of which was myocardial. Five cases showed improvement. Fowler's solution or sodium eacodylate was used in conjunction with the salvarsan in these cases. Four cases treated in the Baltimore City Hospital showed improvement, but one

<sup>1</sup> Medical Record, March 8, 1913.

<sup>2</sup> British Medical Journal, May 24, 1913.

<sup>3</sup> Bulletin of Johns Hopkins Hospital, October, 1913.

relapsed after several days and died of an intercurrent bronchopneumonia. In all of the cases, 0.2 or 0.3 gram of the drug were administered intravenously, with great care as to the dosage and technique. All of the cases showed a sharp febrile reaction in contradistinction to cases of syphilis treated in the same way. They likewise showed a temporary drop in the red-cell count of not more than 200,000. The author believes that the results obtained by the use of this drug justify its further use in pernicious anemia with special attention to (1) the presence of syphilis; (2) influence of salvarsan when given alone; (3) its effect on arsenic refractory cases, and (4) the permanency of the results obtained.

While the foregoing reports give some encouragement to the use of this drug in pernicious anemia, Maynard<sup>1</sup> reports a case in which its administration proved futile. The patient was a male, aged sixty-one years. Two intramuscular injections of the drug were given, with an interval of sixteen days. In two months the erythrocyte count did not rise above 1,334,000. The case is still under treatment with an autogenous vaccine of streptococcus obtained from the gums.

The experience of Nammack<sup>2</sup> agrees with that of Leedle<sup>3</sup> that however useful salvarsan may be in the secondary anemia which occurs in an early stage of syphilis, its use is positively contra-indicated in pernicious anemia occurring in a man in the fifth decade who confesses to luetic infection in early life.

Vogel and McCurdy<sup>4</sup> claim that the *transfusion of physiologically unaltered blood* is one of the most promising forms of palliative treatment available in pernicious anemia. The number of cases on record, in which a remission of notable degree and considerable duration has followed immediately on a transfusion, is so great as to make it impossible to regard these results merely as coincidences. If proper precautions are taken to select a healthy donor, and, by the usual tests for isoantibodies and isoagglutinins, the serum and corpuscles of donor and recipient are found mutually congenial, there is no danger, and the measure should be employed earlier in the disease instead of waiting until the patient is in a desperate condition. There is evidence in favor of the view that greater judgment and accuracy are needed in determining the amount of blood to be transferred. It is quite possible that too large an amount of transferred blood may be injurious, and that more benefit is to be expected from small doses introduced at intervals to be determined by the progress of the patient. The enumeration of the reticulated cells by means of the method of vital staining affords a useful means of gauging the hemopoietic activity of the marrow bone,

<sup>1</sup> British Medical Journal, January 11, 1913.

<sup>2</sup> Medical Record, May 10, 1913.

<sup>3</sup> See PROGRESSIVE MEDICINE, June, 1912, p. 284.

<sup>4</sup> Archives of Internal Medicine, December, vol. xii, p. 6.

and, by watching the patient's progress in this way, the indications for, and effects of, various therapeutic measures can be well determined and supervised.

David<sup>1</sup> confined dogs to a chamber in which the oxygen had been reduced to 10 per cent. and found that there was a marked increase in the number of red cells; and, that this was a real increase of the cellular elements and not a mere decrease in the fluids.

He cites 13 cases, among which were cases of simple anemia, pernicious anemia, and chlorosis, which he treated by allowing them to breathe an atmosphere having only 10 per cent. of oxygen for from one to two hours each day. In all of these cases, he noted an increase in both the red cells and in the hemoglobin.

In various forms of anemia, Zubryzcki and Wolfsgruber<sup>2</sup> advocate the *intramuscular injection* of 20 to 30 c.c. of *defibrinated blood*. The injections are repeated at intervals, as needed; usually three to four days. The authors claim the procedure to be free of all danger, and in the 6 cases in which the measure was carried out at Wertheim's Clinic, the results have been remarkably favorable. The blood-findings in both the patient and the donor are tabulated in detail to show the prompt improvement in the blood-count after the injections. The general health improved correspondingly.

Weber<sup>3</sup> advocates the intravenous injection of small quantities (5 c.c.) of defibrinated blood that has been allowed to stand for twenty-four hours. He warns explicitly against the use of large doses which are liable to give rise to severe reaction. Weber insists that the small amounts are just as effectual as large amounts, and that the benefit derived from this procedure is, at least, equal to that obtained from the use of arsenic.

Windesheim<sup>4</sup> states that prompt improvement followed intragluteal injection of 10 c.c. of still warm human blood at intervals of ten or fifteen days. The patient was a woman, aged fifty-two years, with signs of pernicious anemia, entire loss of appetite, and repeated vomiting. Seven injections of the blood were made in the course of four months, and the blood regained nearly its normal composition and the patient now feels well and comparatively strong.

Parisot and Henly<sup>5</sup> have noted that the resistance of the red-blood corpuscles to injurious influences is increased through the administration of *calcium chloride*. In 14 cases of hemolytic jaundice they gave daily doses of 4 grams of this drug, and, in each case, noted that the fragility of the erythrocytes became distinctly less.

<sup>1</sup> Deut. Arch. f. klin. Med., 1913, vol. cix, 1, 2.

<sup>2</sup> Wien. klin. Woeh., January 16, 1913.

<sup>3</sup> Münch. med. Woch., June 17, 1913.

<sup>4</sup> Ibid., October 7, 1913, vol. ix, No. 40.

<sup>5</sup> Semaine Médicale, February 19, 1913.

This is in accord with the experiences reported by Iscovesco, Taissier, and others, when they encountered increased fragility of the erythrocytes in cases of nephritis. The drug apparently is without any effect in the congenital type of the disease. Improvement in the blood conditions results from the administration of *cholesterin* which has been amply proved experimentally and in the few clinical cases in which this drug has been used to combat hemolytic jaundice.

Cantieri<sup>1</sup> has successfully treated an infant suffering from splenic anemia by the administration of *cholesterin*. The child was eleven months old, with a negative family history. It was healthy until two months before admission to the hospital, when pallor and then abdominal enlargement were noted. There was vomiting, pain, and signs of a hemorrhagic diathesis. The spleen was enlarged, the urine negative, and the feces showed neither blood, ova, nor parasites. The spleen juice obtained through puncture proved negative for parasites. The Wassermann reaction was negative. Upon admission, the blood showed 20 per cent. of hemoglobin, and 1,800,000 red cells; color index, 0.55; leukocytes, 4800. There were moderate anisocytosis and poikilocytosis with slight polychromatophilic; few normoblasts, megaloblasts and erythrocytes showing basic degeneration. The author used the combination recommended by Serona, known as "Coleola," which consists of equal parts of olein and palmatin, ether of *cholesterin*, olive oil and phiolein. Injections of 0.05 of this preparation were given on June 24, 26, 28, 29, and on July 1, 2, 3, 4, 5, 6, and 7. On June 28, the child's weight was 7.5 kg. After the series of injections, improvement was noted; the spleen was smaller, the weight had increased to 8 kg., and the blood showed 75 per cent. hemoglobin; 3,900,000 reds; color index 0.96; 4300 whites; almost no anisocytosis and marked polychromatophilia and basophilia. Beginning July 11, 13 daily injections were given, and on July 27, the weight of the infant was 8.7 kgs. The spleen was noted 1 cm. below the costal margin and the blood showed 80 per cent. of hemoglobin; 4,750,000 red cells; color index of 0.84, and 8800 leukocytes. The morphology of the blood was normal.

**Leukemias.** The studies and reports on the leukemias appearing during the last year show little advance in our knowledge of these diseases. A new type of leukemia coördinate with the splenomedullary and lymphatic forms has been described by Reschad and Schilling. The major portion of the literature of the subject has been in the realm of treatment.

**EXPERIMENTAL.** Wiczkowski<sup>2</sup> has apparently succeeded in transmitting lymphatic leukemia from a man to a chicken by inoculation. In a preliminary communication, the author describes a case of lymphatic leukemia which developed fifteen days after a trauma of the back of the foot. Swelling of the inguinal glands was first noted, followed

<sup>1</sup> Wien. klin. Woch., November 27, 1913.

<sup>2</sup> Ibid., April 10, 1913.

by enlargement of the glands generally, with splenomegaly and enlargement of the liver. There was an ascending temperature and with this a rapid increase in the number of white-blood corpuscles from 27,000 to 590,000. The blood-picture was that of an acute lymphatic leukemia, and the diagnosis was verified postmortem. The blood of the patient, an emulsion of the lymphatic glands, and a portion of the pleural exudate were injected into five chickens. The chickens inoculated with the blood and gland emulsion remained healthy, but the one receiving the pleural exudate became sick, pale, developed edema of the feet and legs, and died. Examination of the blood in this case revealed a large percentage of lymphocytic cells. Postmortem, the spleen and liver showed enlargement, as well as the lymphatic glands. In the liver, also, could be demonstrated collections of lymphocytic cells, especially along the course of the vessels. These lymphocytic cells resembled the cells of the patient, and were not characteristic of chicken leukemia. Emulsions from the spleen, liver, lymph glands, blood, and other organs of this chicken were injected into ten other chickens, and the author promises to report upon the further results of this work.

**ETIOLOGY.** Roth<sup>1</sup> has studied a case of subacute miliary tuberculosis in which the blood-findings were those of myeloid leukemia of the myeloblastic type. After describing the case, with complete postmortem findings, the author enters into an elaborate discussion of the conditions, and concludes by quoting Nana to the effect that tuberculosis in a case studied by him was probably the cause of a chronic myeloid leukemia. Nana cites a number of cases (Quincke, Franchsen, Junger, and Lichtheim) of myeloid leukemia accompanying miliary tuberculosis in which old tubercular foci were found. Roth believes that, if at the present time we cannot go so far as to look upon tuberculosis as the etiologic factor in these cases, yet, as a matter of course, we must not look upon these very frequent complications of chronic myeloid leukemia as unimportant coincidences.

Facchin<sup>2</sup> has found 7 recorded cases of leukemia developing after an accident involving the spleen, including two in which it followed splenectomy; Murrich regarded amputation of the thigh as responsible for the leukemia in a case coming under his observation. In Facchin's 2 cases, the spleen was directly injured in a fall or in an accident bending the body far over backward. The extreme pallor and weakness and the leukemic blood-findings continued a progressive course until each of the young men died of intercurrent pneumonia in about two months after accident.

**PATHOLOGY.** Boggs and Guthrie<sup>3</sup> report 4 cases of myeloid leukemia which they studied with regard to the effect of benzol on the excretion

<sup>1</sup> Zeit. f. klin. Med., 1913, vol. lxxviii, 1 and 2.

<sup>2</sup> Gazzetta degli Ospedali e delle Cliniche, Milan, May 18, vol. xxxiv, p. 59.

<sup>3</sup> Bulletin Johns Hopkins Hospital, December, 1913, vol. xxiv.

of protein. So far as the authors have been able to ascertain, three of their cases are the first reported instances of Bence-Jones proteinuria in association with myeloid leukemia. It has never been observed in the acute forms of the disease, either lymphatic or myeloid, and, including the cases presented here, only eight times in the chronic varieties. The Bence-Jones protein alone was present in 2 cases, while Moner's body also was present in the other 2 cases, as well as serum albumin in one case. The excretion of the Bence-Jones body was small in amount, which seems to be characteristic when it occurs apart from multiple myeloma. The chlorid output was normal in one case, which is markedly different from the condition found in two other cases and in cases of myelomatosis and carcinomatosis. In 2 cases the effect of the benzol treatment is especially noteworthy, in that a marked reduction or eventual disappearance of the proteinuria, and its associated polyuria, occurred, parallel to the diminution in the leukocytosis and apparent approach of the bone marrow to a more nearly normal condition. These cases furnish additional confirmation of the previously expressed view, that Bence-Jones proteinuria is not essentially dependent on one disease, but is a manifestation of disturbances in the bone marrow affecting endogenous metabolism.

An extensive study of the *metabolism in a case of lymphatic leukemia under treatment with the x-ray* has been made by Cavina.<sup>1</sup> He calls attention to the paucity of the literature on this subject. Only four reports have been made, those of Rosenstern (1906), Rosenbaum (1907), Linser and Sick (1907), and Vas (1909). The patient, a male, aged forty-one years, was admitted to the hospital, January 16, 1912. The metabolic studies were carried out from March 12 until April 16, in ten periods. The first period of six days preceded the x-ray treatment. The next four periods of three days each were during the treatment. The next four periods of four days each were subsequent to the treatment, and the tenth period of two days occurred about the middle of May. During this time the hemoglobin advanced steadily from 50 to 60 per cent. The red-blood corpuscles increased from 3,220,000 to 3,980,000, and the white corpuscles showed a steady decrease from 60,860 to 10,780. The daily excretion of urine was somewhat above the normal average throughout, varying from 1844 c.c. to 2130 c.c. The specific gravity showed a fairly steady increase from 1016 to 1021. The acidity of the urine, measured in terms of HCl, in the first period was 1.10. During the periods under treatment, it fell, but rose subsequently to 1.81. The total nitrogen showed a steady increase from 13.12 to 20.94. The urea likewise showed a steady increase from 22.66 to 38.87. The amino-acid nitrogen varied irregularly from .28 to .38. During treatment, the body weight showed a slight diminution from 51.5 kg. to 50.5 kg., but in the subsequent periods there was a

<sup>1</sup> Deut. Arch. f. klin. Med., 1913, vol. ex, 5 and 6.

steady increase in the body weight up to 55 kg. The intake of nitrogen increased throughout on account of increased appetite. This was true of all periods, except in the third, when there was a slight falling off in the intake. The nitrogen balance showed good retention with the exception of the third period, which showed a loss of .76. The retention increased from .59 to 4.24. The phosphorus balance ( $P_2O_5$ ) showed a loss throughout with irregular variations from .33 to .64 with the exception of the fifth period, when there was a retention of .25. The intake of phosphorus throughout was increased on account of increase of food.

The sulphur balance showed retention throughout, with considerable variation, but there was a distinct increase of retention after treatment was begun. The sulphur in the feces was small in amount as in normal adults, and during treatment this amount was further lessened until in the fifth period it was less than 5 per cent. of the sulphur intake. The neutral sulphur in the urine was normal throughout the periods under treatment, and during subsequent periods it fell perceptibly. The author infers from this that if the neutral sulphur holds any relation to the energy of oxidation, as Salkowsky and Rudenko have assumed, then the  $\alpha$ -rays in this case have improved the processes of oxidation. The author believes that the use of the  $\alpha$ -ray in these cases affects not only the blood and blood-forming organs favorably, but likewise the entire organism and its metabolism. The fact that there is a loss in the phosphorus balance is hard to explain, and the author questions whether this loss occurs in all cases of lymphatic leukemia.

Spuler and Schittenhelm<sup>1</sup> have studied the blood from a case of lymphatic leukemia for the purpose of determining the origin of the so-called "kern," or "zellschollen," and the nature of the eosinophile cells. Their studies led them to the conclusion that the bodies designated as "zellschollen," which one finds especially in the blood of lymphatic leukemia, arise from lymphocytes which have a relatively pyknotic nucleus through breaking up of the cell nucleus and the mixing of its constituents with those of the body of the cell. These modified (degenerative forms) of lymphocytic cells arise in the lymph glands. In the lymph glands there are found groups of mitotic cells which prove that the lymphocytes are formed here. The coincidence of the blood-destruction and the formation of the eosinophile leukocytes is distinctly apparent, and the authors are therefore led to believe that these cells do not arise from the bone marrow. The metamorphosis of the cell nuclei is a functional phenomenon. They consider puncture of the bone marrow of decided diagnostic worth.

VARIETIES AND DIFFERENTIATION. Hatjejan<sup>2</sup> reports very favorably his experience with the oxydase reaction. (The technique was described in PROGRESSIVE MEDICINE, June, 1910.) In 5 cases of chronic

<sup>1</sup> Deut. Arch. f. klin. Med., 1913, vol. exx, 1 and 2.

<sup>2</sup> Wien. klin. Woch., April 3, 1913, vol. xxvi, No. 14.

myelogenous leukemia, the reaction was positive. Those cells which are peculiar to the marrow were the only ones to respond. In 5 cases of the chronic lymphatic type, the reaction was negative. The author cites especially a case of leukemic lymphadenosis in which the cells could hardly be distinguished from the myeloblasts and which ran an acutely rapid course. Here the reaction was negative, and postmortem examination revealed the case as one of lymphatic leukemia. Among 5 cases of acute leukemia, the reaction was negative in three and positive in two. Postmortem examination showed the three negative cases to be of lymphatic type, while the two positive cases were of the spleno-medullary type. The author concludes that the oxydase reaction or the reaction of Winkler is a peculiar property of the cells of the medullary system, and the facility of its application recommends it for use in practice.

Dunn<sup>1</sup> regards the occurrence of a positive indophenoloxydase reaction in large non-granular cells in acute leukemia as certain proof of their myeloid nature, and allows a diagnosis of acute myeloid leukemia to be readily made from blood-examination. The oxydase reaction is negative in the more embryonic forms of marrow cells. It is always negative in small myeloblasts, and is probably always negative in the most typical stage of large myeloblasts with uniformly dense basophile reticular protoplasm. When it falls positive in these large non-granular cells, it is associated with alterations in the protoplasm which are recognizable by ordinary staining methods, and which indicate stages of ripening toward the granular myelocytes. Cases of acute myeloid leukemia may occur in which the type of blood-formation is so embryonic that the oxydase reaction is valueless for differential diagnosis, but, even in such cases, the histologic characters of the large leukocytes may render a diagnosis possible. He presents three cases.

The onset and course of the first case were not those of the most acute forms of leukemia, and though serious symptoms existed only for four months, Dunn suggests that it is possible that leukemic changes in the organs had been present with subleukemic blood-picture for some time previously. However, the rise in the number of leukocytes in the circulation appeared with great rapidity, from normal limits to over 200,000 per cmm. in ten days time, and the leukocytes present showed very embryonic character, as nearly 90 per cent. are, in Ehrlich's sense, non-granular. Examination of the blood by ordinary staining methods suggested that these non-granular cells were myeloblasts, and that the myelocytes were developing from them. A certain proportion of typical myeloblasts, such as Naegeli described, were present, and an unbroken chain of transitional forms was observed between these and the granular myelocytes. The oxydase reaction was positive in the great majority of these cells, and positive in greatly varying degree in

<sup>1</sup> Quarterly Journal Medicine, London, April, 1913, vol. vi, No. 23.

different examples, a fact which, Dunn says, confirms the idea that transitional forms of many varying degrees of maturity are represented. The histologic examination of the organs showed that the type of blood-formation was myeloid, as described by Schultze, and the myeloid nature of the deposits was again fully confirmed by the positive oxydase reaction.

The second case presented a typical picture of acute leukemia. Its brief course was marked by hemorrhages into the skin and from the mucous membranes, by fever, and by ulcerative gingivitis. The lymph nodes were not enlarged. The blood-picture showed a considerable increase of leukocytes, of which the great variety were large, non-granular cells. These presented the typical characters of Naegeli's myeloblasts, and the transitional forms between them and myelocytes were present, though scanty. The oxydase reaction conclusively proved the myeloid nature of a certain proportion of these, which differed from the others only by a slight alteration of the protoplasm indicative of ripening. The absence of the reaction from the majority of them Dunn explained by their very embryonic character rather than by pathological suppression of a function already developed. They corresponded accurately with the first type of myeloblasts described in the first case, which also gave negative oxydase reaction. The type of the blood formation in the marrow, in the pulp of the spleen, and in the medullæ of lymph nodes, and the atrophy or inactivity of the lymph nodes, he says, were confirmatory of the view, based upon the blood examination, that the case was one of acute myeloid leukemia.

This case differed from the first case not only in being more acute and of more embryonic type, but also in showing much less advanced changes in the organs. In the cervical lymph nodes, for example, there was little enlargement, and the condition of leukemic infiltration was at an early stage, which rendered possible some observation on its mode of occurrence. It was seen that the lymphatic tissue remained indifferent and was composed of small lymphocytes. The myeloblasts were most numerous in the sinuses and in the neighborhood of these. One or two foci of more massive development of myeloblasts which were present were also in the neighborhood of the sinuses. (Similar foci were observed in the spleen and in mesenteric lymph nodes.) These appearances, so far as they go, were in favor rather of the metastatic origin of the myeloid tissue than of the metablastic development of it from cells previously present in the organs.

In the third case, the Jenner and triacid counts gave almost identical figures: 97 per cent. of non-granular and 3 per cent. of granular cells, and the oxydase reaction was negative in all but the granular cells. Accordingly, this reaction gave no indication whatsoever of the occurrence of transition between the two series, and, so far as it goes, the nature of the non-granular cells remains in doubt. The leukocytes

presented perfectly definite myeloid characters; they corresponded in every detail with those described in the second case. The only differences recognizable between the blood-picture in these two cases were the smaller percentage of granular cells, 3 per cent. in place of 6 per cent., and the less frequent occurrence of definite transition forms, such as cells with looser reticulum or with metachromatic violet granules. Absolute proof of the myeloid nature of the case was impossible in the absence of histologic examination of the blood-forming organs, but the characters of the cell seem too definitely those of Naegeli's myeloblasts to render possible any other explanation. This case Dunn would therefore regard as representing a stage of embryonic blood-formation at which the value of Schultze's oxydase reaction as a test for myeloblasts breaks down.

An extremely interesting case of leukemia has been reported by Reschad and Schilling<sup>1</sup> which they consider to be a new type of the disease coördinate with the lymphatic and myelogenous forms. The patient was a farmer, aged thirty-three years, and married. The disease began about six weeks before coming under observation, with inflammation of the gums, malaise and loss of appetite. After three weeks, small spots appeared over the entire body. Six days before admission he had chills followed by fever, and, on the following day, nosebleed, which was relieved only by tampons. On examination, the patient was pale, and the whole body was covered with small spots of subcutaneous hemorrhage. The gums were pale and ulcerated, and bled on slight pressure. Nosebleed set in upon removal of the tampon. Temperature 38.6° C. There was nothing unhealthy to be found upon examination of the heart, lungs, or liver; nothing of note in the stool, and no blood could be demonstrated there. The urine was very cloudy and strongly acid; specific gravity, 1014. The twenty-four hour quantity was 1500 e.c.; 1 per cent. of albumin, and numerous granular casts and pus cells were found. On May 3, the erythrocytes were 2,245,000; leukocytes, 15,000. In the count of the normal cells, only 1 showed the following relations, 100 cells being counted: Basophiles, 0; eosinophiles, 0; myelocytes, 1 per cent.; metamyelocytes, 8 per cent.; neutrophiles, 47; lymphocytes, 42; irritation forms, 2 per cent. There occurred, therefore, of atypical cells only those forms which showed a moderate grade of regeneration of the neutrophilic elements; and the picture was neither that of myeloid nor lymphatic leukemia. This picture, however, was entirely changed when all the cells were taken into consideration, including the large mononuclears and the transitional forms. A count of 500 cells showed the following relations: Basophiles, 0; eosinophiles, 0; myelocytes, 0.2 per cent.; young neutrophiles, 2.4 per cent.; neutrophiles, 12.8 per cent.; lymphocytes, 12 per cent.; irritation forms, 0.4 per cent.; large mononuclear, 7.4 per cent.; transitional forms, 64.4 per

<sup>1</sup> Münch. med. Woch., September 9, 1913.

cent. The Wassermann reaction was negative, and treatment with salvarsan gave no results. On May 15, ulceration in the mouth was noma-like in character; the breath was very fetid, and, on this date, for the first time, the spleen was palpable. The urine was 3000 c.c. in amount, and contained 2 per cent. of albumin. Erythrocytes were 1,200,000; leukocytes 43,000. A count of 500 cells showed the following relations: Basophiles, 0; eosinophiles, 0.2 per cent.; myelocytes, 0; young neutrophiles, 1.2 per cent.; neutrophiles, 13.4 per cent.; lymphocytes, 10.4 per cent.; large mononuclears, 14.4 per cent.; transitional forms (some very atypical), 59.6 per cent. On May 19, the erythrocytes were 920,000; hemoglobin, 20 per cent.; color index, 1; leukocytes, 56,000. On May 20, the patient died in coma. The histological findings postmortem showed infiltration of the skin with large mononuclear and transitional cells. The bone marrow showed the unmistakable presence of large mononuclear and transitional cells in the vessels. The oxydase reaction was positive in the myeloid tissue, but negative in the large mononuclear and transitional cells. Smears made from the spleen showed almost entirely large mononuclear and transitional cells giving a negative oxydase reaction. On section of the spleen, the follicles could hardly be recognized. The pulp was filled with erythrophages, large clumps of plasma cells and an extraordinary mass of large mononuclear cells. The mesenteric glands showed traces of erythrophagocytosis and normal lymph tissue. The interfollicular tissue was infiltrated with normal myeloid tissue giving a positive oxydase reaction. In the bloodvessels, and spreading from them into the fat tissue, there were collections of large mononuclear cells with a negative oxydase reaction. The liver also showed infiltration with these cells.

The authors consider this case to be one of acute leukemia characterized by a marked increase of the large mononuclear and transitional cells which they term "splenocytes." They term the condition "splenocyte leukemia" or "transitional form leukemia" and classify it as a new system-leukemia coördinate with the myeloid and lymphatic types.

Kraus<sup>1</sup> reports the case of a Russian merchant, aged sixty-two years, who, for three months, had suffered from headache and pains in the limbs, gastric disturbances, anemia, somnolency, depression, and subfebrile temperature; cardiac dyspnea gradually developed, anasarca was present at times; and the spleen increased in size until the longest diameter was about 43 cm. The blood-findings were those of an aleukemic myeloid leukemia, with suggestions of pernicious anemia. The total leukocytes were not above normal, but the number of myelocytes was markedly increased, as were also the young forms of the polymorphonuclear cells, while the polymorphonuclears were reduced in numbers. A peculiar finding in this case was the discovery of cells in the blood

<sup>1</sup> Berl. klin. Woch., August 4, 1913, vol. i, No. 31.

which had every appearance of being endothelial cells. Plesch and Lippmann found similar endothelial cells in the pleural effusion of animals rendered experimentally aleukocytic.

Kraus reiterates in conclusion that myeloid leukemia (myelose) can develop either acute or chronic; with mixed cells or myeloblasts; with or without anemia; with an increased number of the white cells (numerically leukemic) or with a subnormal number of white cells (aleukemic); and as a diffuse or more isolated affection of the bone marrow.

Treadgold<sup>1</sup> reports a case of myeloid leukemia in a child with the blood-picture of so-called megaloblastic degeneration. Clinically, the resemblance to acute leukemia was marked, although the white cells were not at first characteristic of that condition. Accordingly, the diagnosis of leukemia was made; but, before death, the white-cell moiety of the blood became typically leukemic.

There is some difference of opinion as to the existence of leukanemia as a distinct disease entity. Drysdale regards the majority reported under this heading as atypical leukemias; and a small minority, including Leube's, as cases of Addisonian, or secondary, anemia. Melland practically agrees in this view. On the other hand, Bushnell is of the opinion that the term leukanemia is not sufficiently comprehensive, in that the anemia is markedly of the pernicious type, while the leukemia *per se* is minimal. Against this it may be urged that in most cases of leukemia the presence of nucleated red cells in the peripheral blood is an integral part of the disease and the present atypical case serves to emphasize this fact and to show that the "red-cell series" may be definitely, and, perhaps, even primarily, involved in the processes which underlie the production of the leukemic state, and, in the absence of any definite etiologic knowledge, it would, therefore, seem better to try and maintain a rigid distinction between atypical leukemia and Addisonian anemia. The word, leukanemia, might perhaps be maintained insofar as it facilitates reference to the literature of these seemingly border-line cases, but on no other grounds.

Pappenheim<sup>2</sup> is of the opinion that the leukanemias, on account of the accompanying anemia, are to be looked upon as symptomologically distinct varieties of the leukemias. Between pernicious anemia with lymphocytosis, lymphatic aleukemia, leukanemia and leukemia there is a continuous chain of symptomatologic transition forms. However, there is no pathological or nosological relation between pernicious anemia and leukemia.

**SYMPTOMS.** Hersheimer<sup>3</sup> emphasizes that the leukocytes in leukemia are below par to such an extent that they are not able to defend against infections, and hence the leukemic is particularly subject to infectious

<sup>1</sup> Lancet, January 11, 1913.

<sup>2</sup> Folia Hematologica, 1913, Band i, No. 14.

<sup>3</sup> Münch. med. Woch., November 18, 1913, vol. lx, No. 46.

processes. The gums, the throat, and the nose have often been the seat of infectious processes, and 38 cases are on record in which the infectious processes were located in the intestines, the findings suggesting typhoid or paratyphoid ulceration. This was particularly evident in Herxheimer's 3 cases of myeloblast leukemia. One of the cases had been diagnosed typhoid fever until the blood-count disproved this. The intestinal findings were exactly those of typhoid, but all the tests for typhoid or paratyphoid bacilli proved negative. The ulcerations were in the ileum exclusively, and they were evidently the work of the colon bacillus alone.

Moreschi<sup>1</sup> reports the detailed findings in a case of a man, aged fifty-eight years, with intermittent typhoid in the course of lymphatic leukemia, and reports further the effect of antityphoid vaccination in 8 cases of leukemia. The leukocytes dropped the next day, in one case, from 157,000 to 85,000, but soon ran up again to nearly the former figure. In the other 7 cases, they sank merely from 164,000 to 104,000, 219,000 to 109,000; 281,000 to 27,000; 160,000 to 74,000 and from 700,000 to 530,000. Various details are tabulated, and also the findings in nine patients with various other diseases given the antityphoid inoculation. In all these experiences there was no agglutination, either in the typhoid fever or after the vaccination in the leukemias, and there was no temperature reaction to the vaccination. Only one of the leukemias, a child of eight years, showed agglutination at 1 to 10 or 20. The parallel absence of both antibodies and fever is significant, confirming the assumption of a close connection between fever and antibody production. In the two healthy persons vaccinated there was a slight febrile reaction and slight agglutinating tendency, while a pellagrin responded with a marked reaction in both temperature and agglutination. This was also true of the arthritis and gastritis patients.

A case of *nodular leukemia* is reported by Reid, Caldwell and Thomson.<sup>2</sup> The patient, a boy aged ten years, was seen on November 2, 1912, for pain in his right hip and leg. As no improvement followed rest in bed, he was admitted to the hospital on November 13. The pain closely resembled that of right hip-joint disease, and splints were applied; but the pain soon developed in the other side. On December 8, enlarged glands were found before the left lower jaw; and some teeth were loose and were removed. Within a few days, swelling appeared above the right zygoma, and subsequently above the left, and later in the groins. He was rapidly losing flesh, but there were as yet no head symptoms.

On December 15, there was loss of vision in the right eye, and later in the left, and slight proptosis. Some spinal fluid was withdrawn and examined. On December 27, his condition was much worse; he was

<sup>1</sup> Policlinico, Rome, November 9, 1913, vol. xx, No. 45.

<sup>2</sup> British Journal Medical, June 21, 1913.

only partially conscious; he did what he was told if he was given time; his answers were fairly intelligent, but were delayed and were chiefly in monosyllables; there were large symmetrical swellings above each zygoma, and the proptosis was more marked; there were sordes on the lips; the abdomen was full and tender; it was examined with difficulty, but no enlargement of liver, spleen, or kidney was detected; all the lymphatic glands—cervical, axillary, inguinal—were enlarged and shotty; on the skin generally, and on that of the abdomen in particular, there were palpable minute millet-seed-like nodules; there was some head retraction, well-marked Kernig's sign and priapism; he was now blind, and later became deaf; there was also paralysis of both lower extremities, with anesthesia and unconscious action of both bowels and bladder; flexion of legs caused pain; one optic disk presented some neuritis, the other was clear. There was also epistaxis a day or so before death. The temperature varied from 98° F. to 100° F., but on December 26, it began to be sharply intermittent and reached 104° F. on January 1; it was subnormal before death, which took place on January 3. Unfortunately a photograph was not obtained nor a postmortem examination allowed.

*Blood.* The coagulability was delayed; the serum showed distinct lipemia; fat was extracted from it.

|                       |                     |
|-----------------------|---------------------|
| Red cells . . . . .   | 2,800,000 per c.mm. |
| Hemoglobin . . . . .  | 55 per cent.        |
| Color index . . . . . | 1 practically       |
| White cells . . . . . | 5,640 per c.mm.     |

#### Differential count:

|                              |              |
|------------------------------|--------------|
| Polymorphonuclears . . . . . | 12 per cent. |
| Large lymphocytes . . . . .  | 49 "         |
| Small lymphocytes . . . . .  | 17 "         |
| Transitional . . . . .       | 12 "         |
| Myelocytes . . . . .         | 10 "         |

There was no poikilocytosis; nucleated reds were found and no polychromatophilia.

A blood-culture gave a negative result.

*Urine.* No albumin, no sugar, no Bence-Jones' substance. Nucleoproteins were present in rather increased amount.

*Lumbar Puncture.* The fluid escaped at high pressure and seemed almost like pure blood; fat was present in large amount in the serum; a culture gave a negative result.

It was intended to confirm or modify these results of the physical examination and of the blood-count by repeated similar investigations, but the rapid course of the disease prevented the accomplishment.

It might be more nearly correct to use the term "infiltrating leukemia."

and not "nodular;" the collections of cells are not always circumscribed; edematous infiltration may be found about the face, neck, and scalp, and this may at times have a greenish color; definite nodules of fair consistency are most common in the bones, especially those of the skull, but have also been found in the pelvis and vertebral column; they may occur also in the skin and subcutaneous tissue—indeed, wherever lymphoid tissue is found. The nodules vary in size from that of a pin's head to that of a fist. They do not occur in the epidermis, but may ulcerate through it. The color varies from that of the surrounding skin to yellow, red, purple, or greenish. Minute nodules are found on the gums and in the submucous tissue of the alimentary tract. Parkes Weber points out that the premycotic infiltration of mycosis fungoïdes may be sufficient to make the skin fall in rolls, and that this affection corresponds to Kaposi's lymphoderma perniciosa.

The *associated syndromes of leukemia* are discussed by Ward.<sup>1</sup> These are four in number, and, with the exception of one, chloroma, they are not necessarily a part of leukemia, but may be met with in other conditions. These other conditions are rather indefinite when one looks at classical descriptions, and, in consequence, confusion arises. They have been raised to the status of distinct diseases and all classes of cases showing them have tended to be included as examples of these diseases without reference to their proper classification. To exemplify this, the author says that in leukemia there are a great multitude of skin lesions—more or less definite tumor formations—and these may even be preceded by a "pre-fungoid" stage. Such cases have been included in the literature of dermatology as examples of mycosis fungoïdes, and "lymphoderma perniciosa" of Kaposi. But these titles also cover many cases, whatever may be their true nature, that are not examples of leukemia. Many cases so reported are in reality leukemias, but it is not possible to assert that all are.

The four associated syndromes are *chloroma*, *mycosis fungoïdes*, *Mikulicz's disease*, and *persistent priapism*. The first is the syndrome in which one finds symmetrical skull tumors, often of a green color, but not always, and resulting in blindness, deafness, etc. There may be also lesions of other bones, or rather, of the periosteum in other situations. All cases of a green color and some others are examples of leukemia, but a similar syndrome may arise in suprarenal sarcoma. The green color may be found in the marrow, etc., of cases of leukemia which have no skull lesions and may be absent in the skull lesions of other undoubted cases of leukemia. The term, nodular leukemia, has been suggested in order that the existence of tumors might be apparent, while the connection with leukemia was at the same time not overlooked. In the second syndrome, that of mycosis fungoïdes, there are a number of nodules either just under the epidermis or in the deeper

<sup>1</sup> British Medical Journal, July 19, 1913.

subcutaneous tissue that are more or less symmetrically arranged in distribution. They may come and go with great rapidity, but this is by no means always the case. A similar syndrome may occur in cases of sarcoma, but the leukemic nodule very rarely, if ever, ulcerates through the skin, whereas the sarcomatous nodule may easily do so. Mikulicz's disease, or the third syndrome, is characterized by swelling of the lachrymal, parotid and submaxillary glands, which is usually chronic and painless and does not tend to suppurate. As a matter of fact, this symmetrical glandular syndrome is not infrequently of greater extent than would appear, for, besides the glands mentioned, the mammae, ovaries or testes may be affected. The swellings are always symmetrical, and microscopically show an infiltration of the gland substance with cells similar to those seen in the blood. This syndrome is met with in mumps and in some other conditions, but rarely. The fourth syndrome, that of persistent priapism, may be met with in other conditions, but the most common persistent cause, according to Warthin, is leukemia. This, like the others, is of the nature of an infiltration, although some of the infiltrating cells may multiply *in situ* and give rise to more or less distinct nodules standing out from the surrounding infiltration.

"Leukemia, as one of the generalized affections of blood-forming tissues, is distinguished by the type of cell involved. It differs plainly from that met with in Hodgkin's disease or Gauchier splenomegaly. Nevertheless, although constantly different from these, it is not constantly the same. This is because the most specialized cells proliferate first. The stimulus may act on a primitive cell, but at first it is able to send out its children in the clothing to which the world is accustomed. But later, the hurry begins to tell, and the daughter cells are less specialized; later still, the primitive cell itself comes forth and then, as a rule, the patient dies."

Kelly<sup>1</sup> reports a case of lymphatic leukemia which is notable for its low leukocytic count and absence of anemia. The patient was a naval officer, aged forty years. The family history was negative. He had never been sick much since childhood until the past year. In January, 1912, he noticed a beginning enlargement of the abdomen, which gradually increased in size, especially on the left side, until September when splenectomy was performed at Johns Hopkins Hospital. At times prior to the operation he was deeply jaundiced, and had frequent diarrhea, and night-sweats. These symptoms were relieved by operation. In November, 1912, the abdomen again began to increase in size and the respirations became embarrassed. On admission to the Naval Hospital, in December, 1912, the patient complained of weakness, constipation, and dyspnea on exertion. There was swelling of the abdomen and edema of the thighs. The physical examination revealed

<sup>1</sup> United States Naval Medical Bulletin, October, 1913

enlargement of the liver, the border extending 7 cm. below the costal margin, the edge being firm and smooth. The lymphatic glands in both groins were somewhat enlarged, but not markedly so. The axillary and cervical glands were palpable. During his stay in the hospital, the patient was tapped several times. Three blood-counts were made, and the average of these showed 4,600,000 erythrocytes, with hemoglobin ranging from 90 to 100 per cent.

The relations of the white cells were as follows:

|                                | Dec. 5,<br>per cent. | Dec. 20,<br>per cent. | Jan. 21,<br>per cent. | Feb. 12, |
|--------------------------------|----------------------|-----------------------|-----------------------|----------|
| Polymorphonuclears . . . . .   | 20                   | 28                    | 42.0                  |          |
| Small lymphocytes . . . . .    | 71                   | 60                    | 43.5                  |          |
| Mononuclears and transitionals | 4                    | 8                     | 4.0                   |          |
| Eosinophiles . . . . .         | 3                    | 3                     | 2.0                   |          |
| Mast cells . . . . .           | 1                    | 1                     | 5                     |          |
| Myelocytes . . . . .           | 1                    |                       |                       |          |
| Rieder cells . . . . .         | Present              |                       |                       |          |
| Total . . . . .                | 1800                 | 17,500                | 17,500                | 21,000   |

No nucleated red cells were found. The feces were normal and the urine usually contained a small amount of albumin, and, on several occasions, a few hyaline or granular casts. The patient's condition became progressively worse, and he died on February 20, 1912, with symptoms of uremia. At autopsy, the principal findings were enlargement of the lymphatic glands along the sternum, at the bifurcation of the trachea, and along the right side of the trachea. The head of the pancreas was surrounded by a mass of enlarged lymphatic glands and the retroperitoneal and mesenteric glands were greatly enlarged. Microscopically, the liver showed widespread infiltration with lymphocytes, particularly in the periportal areas. A specimen of the spleen obtained from Johns Hopkins Hospital showed infiltration with lymphocytes. The kidneys showed passive congestion and some parenchymatous degeneration. The mesenteric glands were hyperplastic. The diagnosis in this case rests largely on the interpretation of the blood-picture and the pathological findings, rather than upon the clinical picture presented. A definite diagnosis could hardly have been made antemortem.

TREATMENT. The subject of treatment of the leukemias receives attention in the literature almost solely through a consideration of *benzol* in its effects on these diseases. The consensus of opinion seems favorably disposed toward the drug, but there is a pronounced undertone of reservation as to its ultimate merits.

The reports of this form of treatment have been very numerous during the year. The good effects derived from its use, however, may be briefly enumerated as follows: There is a marked reduction of the white-blood corpuscles, and, to a large extent, of the pathologic forms of these cells. This reduction proceeds into the normal limits. There

is a marked increase of the red-blood corpuscles and of the hemoglobin likewise to the normal limits. The spleen decreases in size even to the normal. There is increase of the body weight and marked improvement in the general physical condition. Notable ill or poisonous effects of the drug may lead to glomerular and parenchymatous changes in the kidneys and necrotic changes in the liver; while its effect on the bone marrow may lead to aplastic grave anemia and hypoplastic marrow. These conditions are accompanied by hemorrhagic phenomena. A minor ill effect of the drug is its tendency to produce more or less marked gastric or gastro-intestinal irritation. The dosage is a matter for study and should be adjusted to fit each case. Generally speaking, small doses are to be preferred, not more than 3 grams a day being given, and perhaps the drug should be withdrawn when the leukocytes begin to decline in number, and certainly should be withdrawn when they decrease to the neighborhood of 20,000 or 25,000. In the opinion of a number of authors, the effect of benzol is more or less greatly enhanced by a preceding course of Röntgen therapy.

Koranyi<sup>1</sup> reiterates that his experience, in 6 of 8 cases of leukemia, has been excellent; another patient did not tolerate the benzol, and in the eighth case no benefit was derived from either the Röntgen rays, thorium, or benzol. In the 6 favorable cases, the whites dropped from 200,000 or 300,000 to 4000 up to 12,000. The relative number of the pathologic forms materially declined, the patients were able to return to business, and one woman, received in a miserable condition, is now at the sixth month of pregnancy and seems to be entirely well. Six other clinicians have reported nearly as favorable results. In all the cases, the spleen subsided in size, with the swollen lymph nodes, and the patient increased in weight. In one case the whites increased again to 24,800 by the end of the third month, but, on resumption of the benzol, they dropped again to 6000. Tedesco<sup>2</sup> adds that he has never witnessed any injury of the kidney or impairment of the general health with the maximal dose of 3 gm. per day in the clinic (see PROGRESSIVE MEDICINE, June, 1913, p. 327.)

Kiralyfi<sup>3</sup> emphasizes that, in future, greater caution in the dosage is necessary, as it has been found that certain after-effects will have to be reckoned with. On this account, he now advises to suspend the benzol before the leukocytes have dropped to the normal figure. When the figure has reached 25,000 or 20,000, the benzol should be dropped, or, better yet, it should be suspended as soon as the number of leukocytes starts to decline. Neumann has reported a case in which the leukocytes dropped under benzol from 56,000 to 5000, and later to 200, but the patient's nose began to bleed and the hemorrhage became

<sup>1</sup> Wien. klin. Woch., Vienna, January 23, 1913, vol. xxvi, No. 4.

<sup>2</sup> Ibid.

<sup>3</sup> Ibid., June 26, 1913, vol. xxvi, p. 26.

uncontrollable, the patient dying thirty-nine days after suspension of the benzol.

Kiralyfi had a similar experience with a girl, aged eighteen years, with symptoms of leukemia for two years, and, at the time of treatment, 73,000 leukocytes, great enlargement of the spleen, and temperature up to 40° C., (104° F.). As the patient could not take the benzol by the mouth, it was given in a rectal enema of 2 gm. of benzol in 50 gm. of olive oil three times a day. In a week, the leukocytes dropped to 33,200, and, by the sixteenth day, to 5000, while the spleen subsided in size, the temperature to normal, and the patient felt well. The benzol was then suspended, and the case was cited as a brilliant example of the curative action of benzol. The leukocytes continued to drop until they numbered 2800; then epistaxis commenced and continued for seven days scarcely influenced by local measures and injection of gelatin or serum. With the decomposition of the blood behind the tampons, fever developed, and the patient died, as the heart action grew weaker, the twenty-second day after suspension of the benzol. The leukocytes then numbered only 460; no myelocytes could be found, and there were only 3 per cent. myeloblasts. No other instance of such hemorrhage has been encountered at the clinic. The case teaches that benzol acts by the rectum as effectually as by the mouth, and also that the desired aim should be reached more gradually. Another case reported illustrates the aggravating influence of a pregnancy in the course of leukemia. The patient had been clinically cured by two courses of benzol treatment in about nine months. Then she became pregnant and at term the old leukemic symptoms returned in a more pronounced form (see PROGRESSIVE MEDICINE, June, 1913, p. 328).

Klein<sup>1</sup> reports his experiences with benzol treatment during the last six months in 22 cases of leukemia. He gives full details of 12 cases, and states that the best results were obtained when the benzol treatment had been preceded by a course of Röntgen exposures. The benzol seems then to act much more intensively and more rapidly on the organs and on the blood than either the radiotherapy or the benzol alone. He advocates this combination treatment in all cases of leukemia, especially for those with very high leukocyte count; in one of his cases, the leukocytes numbered nearly a million. He was unable to detect any difference in the effect between the various forms of leukemia, and, although his results were not so encouraging as those reported by Kiralyfi and Koranyi, he thinks that benzol is destined to play an important role in the treatment of leukemia. He did not give as large doses as others, as a rule, finding that the results were equally good with less than 4 gm. per day. Doses up to 5 gm., in a few cases, sometimes had an unfavorable influence on the red corpuscles. He has recently been injecting the benzol subcutaneously, mixed with equal parts of

<sup>1</sup> Wien. klin. Woch., Vienna, March 6, 1913, vol. xxvi, No. 10.

olive oil, 1 gm. once a day. In none of his cases were there any signs of irritation in the urinary apparatus. The action of the benzol seems to be restricted to the blood-forming organs.

Stein<sup>1</sup> reports that a six weeks' course of benzol treatment had such a favorable influence in a case of myeloid leukemia that the leukocytes dropped from 225,000 to normal, and the blood-picture approximated normal, while all subjective symptoms disappeared and the patient gained in weight. She was a woman, aged sixty-seven years, and only slight and transient benefit had been derived from a systematic course of Röntgenotherapy. The benzol was given according to Koranyi's technique, except that it was given in a capsule which did not dissolve until it had passed out of the stomach. The spleen was no longer palpable when the patient was last seen; when the benzol treatment was commenced, it extended below the level of the umbilicus and to the median line. When the benzol was suspended, arsenic was given for a time longer.

In a case treated by Fossati,<sup>2</sup> a fatal outcome seemed imminent when a course of benzol treatment was given and prompt improvement followed. The young woman was not able to bear the large doses of benzol that have been advocated, so the dosage was only from 20 to 60 drops in capsules, suspending the treatment for a day or so occasionally. The temperature returned to normal, and, by the end of two months, the general condition was better than it had been since the first symptoms had been observed a year before. The blood count at various dates is tabulated, showing the increase in the reds and the drop in the whites from 360,000 to 56,000 in three months; the hemoglobin increasing from 35 to 50 per cent.

Wachtel<sup>3</sup> has given benzol in two cases of leukemia. In the first, a severe myeloid leukemia, he was obliged to drop the benzol after the third day as albumin appeared in the urine. The second case resulted in an apparent clinical cure.

Neumann<sup>4</sup> reports from Giessen a case which warns against building too high hopes on the benzol treatment of leukemia. He followed Koranyi's directions giving up to 8 capsules a day, each 0.5 gm., commencing with one twice a day and increasing to two four times a day and then gradually reducing the dose. The course took thirty-six days, and the leukemia was so much improved that the patient felt that she had been cured, but soon after the general health grew worse and worse, fever and diarrhea followed, with repeated epistaxis and a fibrinous and, later, hemorrhagic stomatitis and rhinitis, and the patient died thirty-nine days after the course of benzol. The spleen

<sup>1</sup> Wiener klin. Woch., Vienna, 1913, 5, vol. xxv, No. 49.

<sup>2</sup> Semana Medica, Buenos Aires, September 11, 1913, vol. xx, p. 37.

<sup>3</sup> Deut. med. Woch., Berlin, February 13, 1913, vol. xxxix, No. 7.

<sup>4</sup> Therapie der Gegenwart, Berlin, February, 1913, vol. liv, p. 2.

was unusually tough, and the bone-marrow findings resembled the findings reported by Selling in benzol-poisoned rabbits. It seems evident that benzol is a very effectual remedy for leukemia, but its use requires the greatest caution. It may be wise to drop it as soon as a distinct tendency to improvement becomes evident, without striving for a complete cure.

Pappenheim<sup>1</sup> has noted a glomerulitis and marked parenchymatous changes in the kidneys, and peripheral necrotic changes in the liver lobules of rabbits to which large doses of benzol had been administered. He also observed that while the administration of benzol reduced the number of white corpuscles in the peripheral circulation, numerous polynuclear leukocytes collected simultaneously in the dilated capillaries of the lung, spleen, kidneys, and in the liver. He concluded from this that the peripheral leucopenia was not produced by a destruction of white corpuscles, such as is brought about through the use of thorium or the Röntgen ray, but by a depletion of the peripheral circulation and a massing or collection of these cells in the internal organs, especially the liver. The author has also pointed out that benzol may injure the mucous membrane of the intestinal tract, and that this fact has to be considered side by side with the symptoms caused by administration of benzol, viz., nausea, heartburn, eructations, and loss of appetite.

Sohn<sup>2</sup> has investigated the action of benzol on the metabolism. He made full metabolic observations on three healthy non-leukemic patients and in a case of myeloid leukemia. He gave 3, 4, and 5 gm., respectively, of the drug to the three non-leukemic patients daily. In the first case, after three days there was a marked increase in the excretion of neutral sulphur and albumin appeared in the urine. In the second experiment there was again an increase of neutral sulphur noted, along with a reduction of the urea nitrogen and a smaller increase of the ammonia nitrogen. In the third experiment, similar effects on the metabolism were noted. In the leukemic case, there was a marked increase of the neutral sulphur of the urine, and a diminution of the urea nitrogen. On the fourth day, albumin appeared in the urine.

Sohn calls attention to Pappenheim's conclusion that the peripheral leucopenia resulting from the administration of benzol is not due to a destruction of the white corpuscles, but to pseudoleukocytosis in the liver, and points to the fact that his experiments suggest a similar conclusion. The excretions of uric acid before, and during, the administration of benzol are similar, although the white corpuscles in the peripheral blood of the case of leucopenia were reduced from 58,000 to 5600. The change in metabolism Sohn believes is due to the disturbances in the liver and kidneys, which are indicated by the

<sup>1</sup> Wien. klin. Woch., Vienna, January 10, 1913, vol. xxvi, No. 2.

<sup>2</sup> Ibid., April 10, vol. xxvi, No. 15.

albuminuria, the glomerulitis and parenchymatous changes of the kidney and necrotic changes of the liver observed by Pappenheim in rabbits.

A number of unfavorable reports on the action of benzol have appeared. Quadrone and Buzzano<sup>1</sup> treated four cases of leukemia with benzol without any benefit whatever.

Mühlmann<sup>2</sup> reports a case of leukemia in a man, aged thirty-seven years, with necropsy findings. He was given benzol during nearly six months, to a total of 175 gm. There was marked improvement at first; after three or four weeks the condition was much improved, and the condition continued to improve on suspension of the benzol for two weeks; then the leukocytes began to increase in numbers again but a further course of 40 gm. benzol reduced them to 20,000. Then they again increased and the patient succumbed. Necropsy showed extensive necrosis in the liver.

Jespersen<sup>3</sup> reports a case of very severe myeloid leukemia in a man, aged thirty-two years, rebellious to all measures, including 100 exposures to the Röntgen rays. The man was extremely emaciated and entirely helpless, with fever and hemorrhages, when the benzol treatment was begun. The tenth day the number of leukocytes had dropped from 250,000 to 61,000 and the general condition showed marked improvement. The leukocytes dropped finally to 5000, while the reds had increased from 2,000,000 to 3,500,000, and conditions gradually righted themselves until the man considered himself cured and returned to business. It is possible that the preceding radiotherapy may have prepared the way for the benzol. The prompt and remarkable improvement under it did not last long; the disease flared up again, the leukocytes ran up to 750,000, and the pernicious type of red corpuscles made their appearance. The patient died on the twenty-third day after the recurrence of the symptoms. The dosage of benzol had never been over 5 gm. a day.

In another case treated by Jespersen,<sup>4</sup> the improvement under the benzol was marked, but this patient, too, soon died after a period of uncontrollable nosebleed and vomiting.

Klemperer and Hirschfeld<sup>5</sup> regard benzol as a dangerous remedy, as it caused serious injury in the animal research reported. It reduced the number of leukocytes, but induced such severe necrosis of organs that its use in large doses in therapeutics seems dangerous. It seems wiser to try to stimulate the blood-producing apparatus with small doses.

Meyers and Jenkins<sup>6</sup> conclude that benzol is a valuable addition to

<sup>1</sup> *Riforma Medica*, October 25, 1913.

<sup>2</sup> *Deut. med. Woch.*, Berlin, October 23, 1913, vol. xxxix, No. 43.

<sup>3</sup> *Hospitalstidende Copenhaven*, February 12, 1913, vol. lvi, No. 7.

<sup>4</sup> *Deut. med. Woch.*, July 3, 1913, vol. xxxix, No. 27.

<sup>5</sup> *Therapie der Gegenwart*, Berlin, February, 1913, vol. liv, No. 2.

<sup>6</sup> *Albany Medical Annals*, July, 1913, vol. xxiv, No. 7.

the therapy of leukemia of any kind. It would seem to have no uniform action; in all cases it reduces the white cells, but in some, apparently those with very high counts, it does not reduce the leukocytes to normal, while in cases of 100,000 to 200,000 it may give brilliant results. On the other hand, we may have paradoxic reactions. The red corpuscles and the hemoglobin are usually very beneficially influenced. When Röntgen rays can be used in combination, very favorable results may be obtained, the blood returning to normal, with no persisting myelocytes.

Billings<sup>1</sup> is impressed with the drug as a powerful agent—a two-edged sword, which is apparently a remedy of great promise in leukemia, but which, used carelessly, may defeat the purpose of its use and produce an equally serious condition, namely, aplastic grave anemia, hypoplastic bone marrow and a fatal termination.

Selling states that impure benzol contains nitrobenzol and other products (anilin, etc.), and that anilin is the probable toxic substance producing purpura hemorrhagica, aplastic anemia, etc.

It would therefore be best to use only pure benzol, and to watch its effect by frequent examinations of the patient and the blood. It would also seem wise to err on the side of overcautiousness in size of doses and length of time of use of the drug at any one period, rather than to overuse it with a possible resulting hypoplastic bone marrow and aplastic anemia.

Barker and Gibbes<sup>2</sup> emphasize the facts, (1) that benzol does possess dangerous toxic properties; (2) that its clinical effects are not yet clearly understood, and, (3) that the greatest care should be exercised in its administration. A studious regard for the dosage, as thus far determined, a watchfulness for the manifestations of poisoning that are well defined and easily detected, and a willingness to employ other measures in conjunction with this drug, in Barker's opinion, are means that will serve to give the new treatment a fair trial and prevent its falling into an undeserved disrepute. Certainly, no patient should be treated by benzol unless he can be kept under continuous close observation; for the present, therefore, it may be well to restrict its use to the treatment of patients in hospitals, rather than to run the risks attendant on its extension to domiciliary practice.

In regard to the treatment of leukemia with *thorium-X*, Klemperer and Hirsefeld<sup>3</sup> say that the drug shows an extraordinary symptomatic influence on the myeloid type of the disease in the same way that Röntgen therapy does; but that it has no action on the nature or fundamental character of the disease; and, although it can postpone the fatal outcome, it cannot prevent the same. In lymphatic leukemia,

<sup>1</sup> Journal American Medical Association, February 15, 1913.

<sup>2</sup> Bulletin Johns Hopkins Hospital, December, 1913, vol. xxiv, p. 274.

<sup>3</sup> Therapie der Gegenwart, February, 1913.

it likewise often has a symptomatic influence on the disease in that the lymphatic glands are often reduced in size, but it brings about no fundamental modification of the course of the disease. In this view, Rosenow,<sup>1</sup> who has had a disappointing experience with thorium-X in the treatment of leukemia, concurs.

Gioseffi<sup>2</sup> reports a case of myeloid leukemia treated by the *x*-ray, which showed the typical course under Röntgentherapy, marked improvement at first in both the blood-picture and the general health but then return of the severe symptoms. They subsided anew under repetition of the Röntgen-ray exposures, but Gioseffi is anticipating any day to have the symptoms return, as Röntgenotherapy does not seem to arrest the actual cause of the disease, although it has kept this patient in good condition for a few months. The spleen alone was exposed to the rays three and four times in the course of one and three weeks in the two courses of treatment with two months interval. The patient is an X-para, aged fifty-eight years.

**Hodgkin's Disease.** Hodgkin's disease has received but slight discussion during the year. The question as to whether the process is granulomatous or neoplastic in type is still argued. Some interesting bacteriological studies of great promise have been contributed to our knowledge of the condition.

Oliver<sup>3</sup> in discussing the nature of the disease says that though the process is widely considered neoplastic in the later stages, many consider it originally granulomatous. He describes a number of cases to show that even in the earlier stages properties are observed which can be considered only neoplastic. Hodgkin's disease, according to the author, must be classed with the lymphosarcomata and endotheliomata of the lymph glands as a neoplastic process. The following facts compel this conclusion: (*a*) The similarity, and, in some cases, the identity of the histological process; (*b*) the early and constant development of malignancy (invasion of the capsule and veins); (*c*) the ultimate formation of true metastasis, partly, at least, through the blood-stream. The endotheliomata of the lymph glands are of relatively frequent occurrence and may be classed as endothelioma medullare, endothelioma scirrhosum, and endothelioma cylindricum (Winogradow), or, better, by the classification of Ewing, as diffuse, alveolar and perivasicular endotheliomata.

Motzfeldt<sup>4</sup> regards the disease as a clinical entity with no evidence of its connection with tuberculosis, not even with attenuated tubercle bacilli or of other toxins or Much's granules. He believes that the testimony to date shows that this process resembles the infectious

<sup>1</sup> Münch. med. Woch., October 7, 1913.

<sup>2</sup> Gazz. degli Ospedali e delle Cliniche, Milan, October 2, 1913, vol. xxxiv, 118.

<sup>3</sup> Journal Medical Research, December, 1913.

<sup>4</sup> Norsk. Mag. for Laegevidenskatten, Christiania, November, 1913.

granulomata, and although it does not seem to be of the nature of a neoplasm, yet a malignant nature seems evident.

**Etiology.** In three cases of Hodgkin's disease, Bunting and Yates<sup>1</sup> secured a pure culture of a pleomorphic diphtheroid organism. In two other cultural attempts the organism was recognized, but was not secured in pure culture, and in a sixth case a similar organism, morphologically, was stained in the lesions of a primary intestinal Hodgkin case. The detailed biologic reactions of this diphtheroid organism have as yet not been completely worked out by them. The strain recovered from the second case, however, has been found to grow steadily at 37° C., on the media used to secure the cultures and on ordinary agar-agar. On glycerin-phosphate-agar the growth is almost as luxuriant under strict anaërobic as under aërobic conditions. For luxuriant growth, marked moisture of the medium seems necessary. On a relatively dry medium, growth is slow, and the organisms are found to develop as the long forms, granular, banded, and with many club-shaped involution forms. Branching forms are also noted. These forms are especially well developed on the egg-medium, where they also seem to have a tendency to cohere, so that in stained smears one gets many small groups of organisms radially arranged, with clubbed peripheral elements, somewhat suggestive of a minute actinomyces colony, as seen in section. On moist serum tubes with luxuriant growth, the organisms are short and plump, with polar staining. Many of these forms are coccoid. The authors have noted also, as emphasized by Negri and Mieremet, that, in all old cultures, coccoid forms predominate, and also that large spherical involution forms are present. A colony or a streak, which at twenty-four hours shows entirely the bacillary form, will twenty-four or forty-eight hours later, show an apparent outnumbering of the bacilli by the coccoid elements. The organism stains by the Gram method, though the short, plump forms hold the dye less strongly than the longer bacillary forms. It is not acid-fast. No spore formation has been noted. The growth of the organism is at first glistening and grayish, but becomes more opaque and of a white color. Apparently, depending somewhat upon the reaction of the media, there may be, in some early cultures, a slight greenish-yellow tint produced. Old cultures on glycerin-phosphate-agar become brownish, and the media itself darkens. Gelatin is not liquefied. There is no early change in reaction in litmus milk. Bouillon is not clouded by the growth. Flecks appear along the side of the tube and a slimy deposit gradually accumulates at the bottom. Plate cultures show a rounded colony with quite regular edge, a fine stippling of the growth and a central dark spot. The colonies are of a glistening gray color at the end of twenty-four hours, becoming gradually of an opaque white color. Altogether, these studies thus far seem to indicate that

<sup>1</sup> Archives Internal Medicine, Chicago, August, 1913, vol. xii, p. 2.

the authors were dealing with the same organism described by Negri and Mieremet.

In order to determine the possibility of an etiologic relationship between this organism and the disease, Bunting and Yates<sup>1</sup> have inoculated a Macacus monkey with cultures of the organism obtained from a patient in the Mayo clinic. They have produced, in the lymph nodes of the monkey, a chronic lymphadenitis with atypical proliferation of the endothelial cells, a beginning proliferation of the stroma tissue, and a well-marked eosinophilic infiltration; also a periglandular sclerosis. Clinically, the animal's blood has shown an absence of polymorphonuclear leukocytosis after injection of the organism. An increasing percentage of mononuclear elements was found, particularly of the transitionals, an increase in eosinophiles following a primary fall, and an early increase in basophiles, all of which are characteristic of the early stages in Hodgkin's disease. The blood-plates were numerous and large forms were present.

With the picture in the lymph nodes so similar to that of the early stage of Hodgkin's disease in the human being, and so different from an example of subacute lymphadenitis in the mesenteric lymph nodes of a monkey which died of dysentery, and with the blood-picture showing the changes of human patients with the disease, the authors feel more assured of the etiologic relationship of the organism, which they have designated *Corynebacterium hodgkini*, to the disease.

Wade<sup>2</sup> describes a case of Hodgkin's disease of the Dorothy Reed type which was primary in the spleen. He concludes that primary Hodgkin's disease of the spleen is a condition quite unique; but that it occurs no more frequently than has been held is doubtful, since some of the reported cases of primary splenic sarcoma may easily have been unrecognized Hodgkin's disease. In view of our ignorance of the etiology of the condition, and of the fact that the process occasionally arises in other deep-seated lymphadenoid tissues, the possibility of a splenic origin cannot be denied. In the present case, since there was at no time any enlargement of the superficial lymphatic glands, or any evidence of lymphatic hyperplasia in the mediastinum or abdominal cavity; and, since the disease was of long standing in the spleen, as evidenced by the gross and histopathologic appearances, it should be considered one of primary Hodgkin's disease of the spleen, even though no autopsy was held.

TREATMENT. On the basis of the work of Bunting and Yates and Negri and Mieremet, Billings and Rosenow<sup>3</sup> have succeeded in isolating from the lymph nodes of 12 cases of Hodgkin's disease, the organism described by Bunting and Yates in 3 cases in pure culture, and in the

<sup>1</sup> Journal American Medical Association, November 15, 1913.

<sup>2</sup> Journal Medical Research, December, 1913.

<sup>3</sup> Journal American Medical Association, December 13, 1913.

other 9 in conjunction with the staphylococcus. Vaccines of this organism were prepared by growing on the surface of Loeffler's blood-serum, ascites, dextrose and agar, or blood-agar slants for from twenty-four to forty-eight hours. A suspension in salt solution was then made; the clumps broken up as much as possible and thrown down by fractional centrifugation. This clump-free emulsion was then standardized and heated to 60° C., for thirty minutes or an hour. From this emulsion, aërobic and anërobic cultures were made on Loeffler's blood-serum and incubated at least three days before the vaccines were used, in order to insure sterility; 0.5 per cent. of phenol was added and the killed suspension placed in the ice-chest for use. Whenever staphylococci were found, an attempt was made to have the vaccine contain the bacilli and cocci in about the same proportion as they were found in the lymph nodes. Although it is obvious that an autogenous vaccine is to be preferred, good results have been obtained with the vaccines prepared from a series of strains isolated from different cases. Seven of the patients were treated at the Presbyterian Hospital, of Chicago, and were kept at rest. Five were under the care of physicians at home. Röntgenotherapy was applied three times a week to six of the hospital patients and was used with three of the patients under the management of others. Autogenous vaccine was used in all but one patient who received the vaccine prepared from other patients. The vaccine was first given in the dose of from 5,000,000 to 10,000,000, and gradually increased to a maximum of 100,000,000. It was given subcutaneously and repeated every five to seven days. In the febrile patients, the second or third day was associated with a reaction consisting of an increase of temperature, rapid pulse, and general weakness and discomfort. In non-febrile patients, only slight general reaction may occur. At the point of injection there occurs but a slight local reaction. In six of the hospital patients there was a uniform and relatively rapid decrease in the size of the lymph nodes—one of these without Röntgen treatment. One patient treated out of the hospital without Röntgen therapy with very large lymph nodes, big spleen, and febrile, had a violent general reaction with the third vaccination, then became afebrile and the swellings of the lymph nodes and splenomegaly rapidly diminished. After five vaccinations, this patient passed from control and observation. Reports from physicians on two of the series showed favorable progress, with gradual diminution of the tumors, and lymph nodes, and improvement in a general way. One of these patients received Röntgen treatment also; the other, vaccine treatment only. One patient, with rapid enlargement of the mediastinal nodes, died after the third vaccination from the result of mediastinal pressure. The authors use Röntgen treatment conjointly with the vaccines because they believe they would not be justified in depriving the patients of any and all sources of help. If this organism finally proves to be the

cause of Hodgkin's disease, the use of the specific vaccines without  $x$ -ray treatment may then be justified.

**Polycthemia.** The literature of the year on polycthemia has been very small in amount, and nothing noteworthy has been developed in regard to this disease. Cases have been reported by Moewes,<sup>1</sup> Watson and Wemyss<sup>2</sup> and Monro.<sup>3</sup> The latter author cites three interesting cases illustrating various types of this affection. Chauffard and Troisier<sup>4</sup> describe a case complicated with ascites.

Friedman<sup>5</sup> has published a paper on "*A hitherto undescribed form of polycthemia and its possible relation to duodenal ulcer, chronic pancreatitis, and disturbance of internal secretions.*" The material studied by Friedman consisted of 25 patients, 23 of whom were males, and 2 females. The ages ranged from nineteen to fifty-seven years. All of the patients complained of the usual symptoms of chronic indigestion and of attacks of pain. The paroxysmal pain dated back mostly for years, and, in a large number, constant pain was also complained of. Many complained of night-pain; some of hunger-pain; others of both. A large number of them were users of bicarbonate of soda, which remedy they took at night on account of pain, or upon retiring in order to avoid night-pain. Jaundice could not be elicited from a single history. Objectively, there could be demonstrated in all the cases tenderness of different intensity to the right of the epigastrum, in the continuation of right parasternal line somewhat above the navel; in but a few instances tenderness was found also somewhat to the left of the navel, and in one patient there was also tenderness in the appendicular region. In none of the patients was the liver border palpable, or the spleen enlarged, or the gall-bladder palpable. There were no tender spots characteristic for gall-stone disease or for gastric ulcer. Hyperacidity was noted in all, except for one case of hypo-acidity and for another of heterochylia. The presence of occult blood could be demonstrated with the guaiac test only in a small number of cases, though with benzidin more frequently. A complete analysis of the feces of three patients showed pancreatic insufficiency. One of these cases came to autopsy, and was proved to be chronic interstitial pancreatitis. Urine was negative except for a large sediment of phosphates in some, and transient glycosuria in two. The author concludes that polycthemia is apparently a frequent phenomenon in cases of non-bleeding duodenal ulcers, proved such by operation, or answering the clinical syndrome erected by Moynihan and others.

No such phenomena are seen in gastric ulcer. Injection of adrenalin

<sup>1</sup> Deut. Arch. f. klin. Med., 1913, vol. exi, 3 and 4.

<sup>2</sup> British Medical Journal, April 5, 1913.

<sup>3</sup> Lancet, April 12, 1913.

<sup>4</sup> Presse Medicale, August, 1913.

<sup>5</sup> Medical Record, 1913, vol. lxxxiv, No. 16.

in such patient is followed by a transient diminution in the red cells, but, soon after, the polycythemia asserts itself.

Injection of adrenalin in dogs produces a polycythemia which apparently is due to a lesion of the bone marrow. Friedman assumes that the causes of polycythemia in his cases are intimately connected with the causes of duodenal ulcer, and may be due to some alteration in the secretion of adrenalin.

It may be assumed that duodenal ulcer is perhaps a trophic disorder due to some disturbance in the secretion of adrenalin. The author's hypothesis is that adrenalin in such cases acts hormone-like in a specific manner, upon the vessels of the duodenal mucosa and produces the changes that finally lead to the appearance of ulcerations.

Parkes Weber,<sup>1</sup> whose writing on this disease has been so notable, has contributed a paper on the prognostic significance of secondary polycythemia in cardiopulmonary cases. To the question: Is polycythemia a good or bad sign in cardiac cases? the author, in a previous paper, answered as follows:

"Just as hypertrophy of the walls of the heart is useful insofar as it compensates for mechanical defects in the valvular apparatus, so also is polycythemia useful insofar as it compensates for difficulties in the oxygenation of the blood and tissues of the body; but just as in cardiac valvular disease great hypertrophy of the heart indicates some grave defect in the valvular mechanism, so also an extreme increase in the number of erythrocytes in the blood-points to there being great impairment of the normal process of oxygenation of the body."

With the cardiopulmonary cases, however, the author feels that the prognostic significance of the polycythemia is somewhat different; or, as he prefers to put it, "the outlook is exceedingly grave at the stage of the disease when cyanosis and a great degree of polycythemia become striking clinical features." A typical history of the kind of cases to which he refers is somewhat as follows:

The patient, more frequently a male, and at about middle age, has been accustomed to attacks of asthma and bronchitis and has signs of emphysema of the lungs. He has been subject to "colds" and bronchitis in winter, which have frequently lasted a long time. Sometimes there is also a history of past attacks of pleurisy or pneumonia. On the whole, however, he has managed to keep on fairly well with his business and other occupations. But at last, probably during one of his winter attacks, his cyanosis attracts attention, and becomes a marked feature of the case. His cheeks, nose, ears, lips, tongue, soft palate, and fauces are all livid, and so are his hands, though the degree of blueness varies from time to time, from day to day, or from hour to hour, according to temporary conditions of his circulation associated with the state of the weather, the temperature of the room, the amount of bronchitis,

<sup>1</sup> Lancet, May 10, 1913

etc. The conjunctiva may be reddish and suffused, as in cases of splenomegalic polycythemia (erythremia). The short acute paroxysms of asthma, to which he probably used to be subject, become less frequent or no longer occur. But there is often more or less chronic dyspnea and wheezy breathing. When his blood is examined there is found to be a decided polycythemia, so that the number of red cells may reach 7,000,000, or more, to the cubic millimeter of blood. There is no longer the same tendency to recover, or the recovery is likely to be only temporary, and an attempt to resume anything like his ordinary mode of life and daily occupations leads to a relapse. The right side of the heart is hypertrophied and more or less dilated, as may be shown by Röntgen-ray examination. The brachial systolic blood-pressure is rather low, or at least not excessive, unless there are special complications, namely: decided arteriosclerosis or chronic interstitial nephritis present. The fingers are often "clubbed." Usually the liver becomes enlarged, and often slight ascites develops. Occasionally, the ascites may be much greater, needing tapping, and there may be more or less general edema. With increasing cardiac failure, orthopnea becomes more marked. With increasing cyanosis and chronic carbonic acid poisoning, there is often remarkable somnolence, and the sleepiness may progress to actual coma (the so-called "cyanotic coma.") Toward the end there may be epileptiform twitchings or convulsions. Death may be due to actual carbonic acid poisoning or to intercurrent bronchopneumonia, or other intercurrent affection, or may be due to gradual cardiac failure. In regard to the etiology, former abuse of alcoholic drinks, sometimes plays a part, in addition to asthma, pulmonary emphysema, chronic bronchitis, old bilateral pleuritic adhesions, chronic interstitial pneumonia, and pulmonary fibrosis.

As to treatment, some of the cases improve (at least temporarily) under prolonged rest in bed, small doses of potassium iodide, cardiac stimulants, diuretics and expectorants, oxygen inhalation, and perhaps, also, blood-letting.

TREATMENT. Kiralyfi<sup>1</sup> has met with success in the treatment of two cases of polycytemia with benzol. In the first case, at the beginning of treatment, 5600 whites and 17.8 gm. hemoglobin (Fleischl-Mischer) were present. After five months of treatment with benzol at intervals, the red cells numbered 4,810,000 and the white cells 8800. Five weeks thereafter, during which interval no benzol was administered, the red cells numbered 5,170,000 and the leukocytes 10,000. In the second case, at the beginning of treatment the blood-count was 6,500,000 erythrocytes, 10,600 leukocytes, and 120 per cent. of hemoglobin (Fleischl). After three weeks of treatment, during which the patient received 3 gm. of benzol *per diem*, the red cells numbered 4,700,000; the white cells 9300, and the hemoglobin showed a percentage of 105.

<sup>1</sup> Virchows Archiv, 1913, vol. cxxiii, 1 and 2.

Four weeks after the cessation of treatment, the count was 4,960,000 erythrocytes; 5600 leukocytes, and 100 per cent. of hemoglobin.

**Hemorrhagic Diseases.** During the past year the literature on the hemorrhagic diseases has not been very extensive. However, some very interesting work has been contributed, and, in the light of this, our knowledge of these diseases seems in a fair way to advance.

Riebold<sup>1</sup> relates the histories of two families in which *hemophilia* was present, and enters into an elaborate discussion of the factors at work in the transmission of this disease from the standpoint of the Mendelian law. He concluded that the mode of transmission of hemophilia follows throughout the Mendelian law, with the reservation that in general, the disease is dominant only for the male and recessive for the female; and with the further reservation that in some cases, we do not know whether these appear frequently or not, the dominance of the disease for the male can be lost. This latter form of the mode of transmission which has developed from the typical form and can always be traced back to it, appears to be distinctly familial. In certain families where it appears, the men possess the normal condition as a dominant over the disease and transmit this to their offspring. In these cases hemophilia has become a recessive character for all members of the family, and the disease makes its appearance only when both parents possess latent fundaments of the disease, and this nearly always occurs only when marriage takes place between members of the family.

Whipple<sup>2</sup> has continued his interesting work of last year, and, in a paper on hemorrhagic disease, discusses the *antithrombin and prothrombin factors*. He studied 7 cases of various types of bleeding and from these studies draws the following conclusions:

The antithrombin-prothrombin balance in the blood is in delicate equilibrium, but, under normal conditions, there are strong factors which can preserve this balance. Under experimental conditions this may necessitate rapid neutralization of antithrombin excess; again a rapid production of fresh antithrombin or prothrombin. There are wide margins of safety in the normal animal.

This antithrombin-prothrombin balance may be temporarily or permanently upset under disease conditions as reported. The *prothrombin* factor is rarely involved, but it may drop to zero or to a low level which will be associated with hemorrhagic symptoms.

The *antithrombin* factor is frequently involved, and, if this element is much increased above normal, there will be a tendency toward hemorrhage, purpura, etc., depending in part on the duration of the change, but especially on the amount of antithrombin excess.

It may be assumed that during these wide fluctuations of *antithrombin* it may fall *below* normal, whereupon there would be a tendency to

<sup>1</sup> Med. Klinik, April 27, 1913.

<sup>2</sup> Archives Internal Medicine, December, 1913.

vascular thrombosis. Given a low antithrombin content a minor injury to the intima might initiate a thrombus which would grow rapidly. With the growth of a thrombus there would be the formation of much thrombin which would escape into the blood and stimulate the organ (liver) producing antithrombin. This might result in an antithrombin wave—a period of antithrombin excess which would check the growth of thrombi and give the endothelium opportunity to cover over the fresh thrombi, thus removing the foci of thrombin formation. The antithrombin wave may fall promptly to normal or persist for weeks, but, if its duration is a matter of days, there will appear signs of hemorrhagic disease.

It seems highly probable that, under certain conditions, liver injury or disease may be associated with an excess of antithrombin in the blood capable of giving hemorrhagic symptoms. Also certain substances in the blood (peptone, thrombin) will bring about an overproduction of antithrombin due probably in great part to stimulation of the liver. Under this heading may be grouped cases of septicemia (reported previously), pneumonia (Dochez), endocarditis, miliary tuberculosis, generalized vascular thrombosis, etc.

True hemorrhagic disease is rarely associated with simple obstructive icterus, contrary to common belief. Delayed coagulation time in jaundice may be influenced favorably by calcium, but such cases do not suffer from bleeding unless there is some other abnormality—for example, an excess of antithrombin. In these rare cases of true hemorrhagic disease associated with profound icterus, we may presuppose some liver disease and an upset in the antithrombin-prothrombin balance. Calcium has no effect on this condition.

Disease of the blood-forming organs may present symptoms of hemorrhagic disease (aplastic anemia, and leukemia) because of an excess of antithrombin in the blood. It is unlikely that the blood-forming tissues are directly concerned in the antithrombin production as this element is much in excess in the case of anemia, with complete marrow aplasia. It is possible that the products of blood-cell disintegration may stimulate an overproduction of antithrombin. It will be recalled that purpura and hemorrhagic tendencies are more common in acute leukemias in which the evidences of blood-cell disintegration are most marked. It is probable that the majority of hemorrhagic cases and purpuras associated with leukemias and anemias belong in the antithrombin group.

The disease called *melenia neonatorum* in many, perhaps all, instances is characterized by a relatively sudden disappearance of prothrombin from the blood. This condition usually develops during the first two weeks of life and is often fatal. The cases react favorably to fresh serum treatment.

Treatment of hemorrhagic disease should follow a careful analysis of the blood, as harm can be done by faulty treatment. In cases of low or absent prothrombin, it is clear that serum which is rich in this element is indicated, and, in many cases, produces almost miraculous cures. It should be given intravenously, if possible. Direct transfusion is of even greater value.

Treatment of antithrombin cases offers great difficulties. Serum treatment offers no help, and it may even stimulate a still greater over-production of antithrombin. Indirect transfusion is open to the same criticism, as large amounts of thrombin are introduced. It may be possible to find some safe way to introduce thromboplastin into the blood-stream in the hopes of neutralizing the antithrombin excess. If the means by which the antithrombin is neutralized or used in the normal body can be found out by various animal experiments, the solution of this problem in treatment of antithrombin cases may be reached. At present, direct transfusion seems to offer the greatest hope of permanent benefit.

Austin and Pepper<sup>1</sup> contribute a paper on Experimental Observations on the Coagulation of Oxalated Plasma with a Study of Some Cases of Purpura. Their results are presented under two headings: (1) Experimental Studies; (2) Clinical Studies. Of the 12 patients studied clinically, 5 showed purpura, 1 jaundice, and 1 severe anemia. The other 5 were controls of various kinds. From these studies they conclude that a solution of hemolyzed blood-cells is the most readily prepared and active thromboplastic solution. A delay in coagulation time of oxalated plasmas occurs on heating or standing. This is due to the formation of antithrombin, and to the union of antithrombin with prothrombin. The coagulation time in such plasmas is greatly hastened by the addition of thromboplastin solution. The presence of hemoglobin in plasma is a source of error in the determination of fibrinogen by Whipple's method. No method of study has as yet offered as satisfactory an explanation of purpura.

The scheme presented by Austin and Pepper for the study of clinical cases is easily carried out and covers the essential points included in the present knowledge of this subject. In this scheme they take advantage of the thromboplastin solution for demonstrating the presence of prothrombin combined with antithrombin, and they believe that this is an excellent method for detecting an increase in the antithrombin of the blood. The thromboplastin solution is prepared by bleeding a normal dog, which has been starved for twenty-four hours, into a 1 per cent. sodium oxalate solution in the proportion of nine parts of blood to one part of 1 per cent. sodium oxalate. This mixture is immediately centrifugalized and the clear plasma drained off and preserved. The cells are washed three times with 0.85 per cent. sodium chloride

<sup>1</sup> Archives Internal Medicine, March, 1913.

solution and then diluted with three volumes of distilled water. When hemolysis has occurred, 0.85 gms. of sodium chloride are added for each 100 c.c. of distilled water. For the clinical study of coagulation they suggest the following steps, in addition to a complete blood-count and a careful enumeration of the blood-platelets:

1. Estimation of the coagulation time of a drop of blood from the finger with one of the clinical coagulometers.

2. Take 20 c.c. of blood from a vein of the arm and mix with 2 c.c. of 1 per cent. sodium oxalate solution and centrifugalize.

(a) To 1 c.c. of plasma so obtained, add 0.3 c.c. of a 2 per cent calcium chloride solution and determine beginning and complete clotting. If delayed,

(b) To 0.75 c.c. of the original plasma add 0.25 c.c. of blood-cell solution prepared as described and 0.3 c.c. of 2 per cent. calcium chloride and determine beginning and complete clotting. Again, if delayed,

(c) To 0.5 c.c. of plasma add 0.5 c.c. pure fibrinogen solution, and 0.3 c.c. of 2 per cent. calcium chloride solution, and determine beginning and complete clotting.

A delay in (1) but not in (2-a) suggests that there is not sufficient calcium available in the blood for normal coagulation, but that the other constituents are normal; a delay in (2-a), but not in (2-b) suggests that much of the prothrombin present is bound by antithrombin and is, therefore, inactive.

A poor coagulation in (1), (2-a) and (2-b), but good in (2-c) suggests that there is a deficiency of fibrinogen which can be further confirmed at (3). (See below.)

A delay in (1), (2-a), (2-b), and (2-c), suggests a deficiency of prothrombin bound or unbound, with, or without, a deficiency of fibrinogen.

3. Precipitate fibrinogen in 10 c.c. of plasma by heating to 58 to 60° C., for fifteen minutes on a water bath. Centrifugalize in a graduated tube for twenty-five minutes and read the amount of sediment in volume per cent. This method is useless if plasma is discolored with hemoglobin.

It may be noted here that a pure filmy clot may result quite as readily from a lack of prothrombin as from a lack of fibrinogen in spite of statements in the literature to the contrary. According to the authors, they have repeatedly observed this type of clot in working with solutions of pure fibrinogen in abundance but containing only a trace of thrombin.

Barratt<sup>1</sup> has studied the effects of the intravenous injection of thrombin and thrombokinase in rabbits. He finds that, when these substances are injected, fibrin separation begins in the circulating blood. The action of thrombin in all of these cases is the immediate cause of this separation. Depending upon the rapidity of the formation of fibrin,

<sup>1</sup> Journal Pathology and Bacteriology, Cambridge, January, 1913.

it occurs as clots in the heart, especially of the right side, and great vessels, following the course of the injected fluid; or, masses of it appear in the smaller bloodvessels and capillaries. If the separation of fibrin is very rapid, clotting occurs both in the heart and great vessels, and in the smaller bloodvessels and capillaries. If the process is relatively slow, it occurs only in the smaller vessels. Mechanical interference with the circulation explains in part, if not wholly, the symptoms produced. There is no evidence that the injected fluid causes any additional toxic effects.

Cousin<sup>1</sup> describes three cases of purpura which illustrate a familial tendency to this disease. The first case occurred in a child, aged ten years. Three years later a cousin rapidly developed the disease at about the same age, and four years later a more distant cousin was taken with the disease. There is no history of hemophilia in the family, but there is a distinct tendency to bleed easily. Calcium chloride, in all three cases, was effectual in promoting a cure, with no return. The author states that two of the children are now sturdy youths, but that the third is inclined to be delicate.

TREATMENT. In the treatment of hemorrhagic diseases the use of *blood serum*, especially human, and of *human whole blood*, has proved successful in numerous cases reported through the past year. Other forms of treatment have been used with success. Our present knowledge of these diseases, and especially the means at our command for studying the blood with the view of ascertaining what constituents are needed to bring about fibrin formation, places us in a position to treat these diseases with more or less accuracy and attending success.

The treatment of the hemorrhagic diseases of the newborn by means of *human serum* is discussed rather fully by Welch.<sup>2</sup> He takes issue with the view that in the injection of serum certain substances are introduced which bring about coagulation. These substances he holds would act as an antigen and stimulate the production of an antibody which would neutralize them. The hemorrhages, according to him, are not controlled by a coagulation process. Human serum as a controlling agent seems to perform its function by virtue of its food value. It contains molecules which the deranged cells, both endothelial and general, can readily assimilate by absorption or osmosis and thereby easily restore equilibrium. In the case of the endothelium, by rendering the inner wall of the bloodvessel impervious to blood and restoring the power of the general tissues to produce thromboplastin, thereby reducing the coagulation time to normal in those cases in which it has been delayed. Clots do not form in the bleeders in which hemorrhage has been controlled by human serum injections. On the contrary, the hemorrhages are quickly absorbed without clots appearing.

<sup>1</sup> Annales de M.-L. et Chir. Infantiles, Paris, October 1, vol. xvii, No. 19.

<sup>2</sup> New York State Medical Journal, November, 1913.

Welch's technique is as follows: Into a heavy glass filter flask of about 400 c.c. capacity, a rubber stopper having two perforations is fitted. Through one perforation is inserted a short glass tube containing a piece of cotton. Through the second perforation is inserted a U-shaped glass tube to the outer end of which a needle, caliber No. 19, is attached by means of a piece of soft rubber tubing. The outer end of the U-tube carrying the needle is then cotton plugged into a small test-tube, and the entire apparatus sterilized at 150° dry heat for half an hour.

In the preparation for withdrawing the blood, a tourniquet is placed around the arm just above the biceps and pressure enough exerted to almost obliterate the radial pulse. After extreme engorgement of the veins has been produced, the needle of the apparatus is inserted in a prominent vein at the elbow and about 10 ounces of blood withdrawn into the flask. The rubber stopper is then withdrawn and a sterile cotton plug inserted in the flask which is then placed in a slanting position at room temperature (not on ice) until the coagulum has contracted and expressed the serum which can then be decanted into a sterile flask and placed on ice for use as desired. Enough serum will collect in one hour for an initial injection, and the beginning of the treatment need not be delayed longer.

In giving the injections, it is advisable to use a glass syringe which can be thoroughly boiled, as the use of chemicals in the sterilization of the instruments might cause alteration of the serum, thereby neutralizing or rendering it toxic. One ounce of the serum is given at each injection twice daily to moderate bleeders. To those bleeding profusely, it should be given three times daily or every four hours until the bleeding is under control, which is usually within twenty-four hours. The serum is best given subcutaneously, very slowly and with gentle massage over the site of administration until all of the amount injected shall have been taken up by the circulation.

Hahn<sup>1</sup> reports two cases in which, as a last resort, the bleeding gum was cauterized with the *thermocanterry*. This seems paradoxical treatment, as a cautery must open new vessels. The prompt success in both cases shows that under the influence of the heat the contents of the vessels must have coagulated and the production of the thrombi from the changes in the vessel must have aided in preventing further escape of blood. It is possible also that the necrosis of the tissues liberated substances which promoted local coagulation. In one of his cases, the child had injured its mouth in a fall and the bleeding had kept up for seven days, uninfluenced by injection of antitoxin, horse serum, and gelatin. To prevent the child from working off the seab after the cauterization, a bandage was adjusted to protect the upper lip and gum. In addition, 15 c.c. of fresh human blood was injected into the

<sup>1</sup> Münch. med. Woch., May 6, 1913, vol. lx, No. 18.

nates. There was no further hemorrhage in either case after the cauterization.

Mankiewicz<sup>1</sup> reports two cases in young men who had histories of serious hemophiliac hemorrhages in previous years; in both, the hematuria came on a few hours to two days after a steam bath with massage or a superheated air bath. The urine filtered without leaving any sediment, so that there must have been hemolysis. One patient was quieted with morphine, and the tendency to hematuria subsided under gelatin internally, ergot, epinephrin, and castor oil. This patient died suddenly a few months later from acute heart failure. The hematuria kept up in the other patient notwithstanding the usual measures, including the subcutaneous injection of horse serum. Then, at a consultation, Kussmaul's old experience was recalled: he failed constantly on account of hemorrhage, in some experiments on dogs, until he kept the dogs from drinking, feeding them abundantly, but giving them little, if any, water. On this dry diet the blood became so much thicker that there was no further tendency to hemorrhage. Mankiewicz acted on this suggestion in this rebellious case of hematuria, and the hematuria ceased as the patient refrained from fluids. He had the heroism to refrain for two weeks from drinking, and his food was prepared as dry as possible. The blood and organic juices thus became more concentrated, and contained proportionately more coagulable substance. The result was complete subsidence of the manifestations of hemophilia. The young man has kept up the gelatin by the mouth to date; it was given by subcutaneous injections during the first four weeks. The success in this case justifies the systematic, protracted administration of gelatin, in connection with a dry diet, as the routine treatment for severe uncontrollable hemorrhage in general, and particularly when the patient is a "bleeder." Even the simple technique for transfusion may prove a dangerous operation in a hemophiliac.

Nobecourt and Tixier<sup>2</sup> report a case of familial hemophilia in which repeated subcutaneous injections of a 5 per cent. solution of peptone (Witte), kept the tendency to hemorrhage under control. The boy, aged ten years, was given sixty-seven injections between May, 1910, and October, 1912, series of three or four injections being given at intervals, or when there was extravasation of blood in a muscle or joint. At first the blood showed no sign of coagulation for three hours, and the venous blood did not clot for twenty-four hours, but after treatment blood from the finger began to clot in twenty minutes and coagulation was complete in five more minutes. The reds numbered 4,576,000, whites 9000, and the hemoglobin was 95 per cent. Injections of serum had proved ineffectual in this case, and in the course of time the peptone seemed to prove less effectual as a preventive of accidents, although retaining

<sup>1</sup> Zeit. f. Urologie, Berlin, November, 1913, vol. vii, No. 11.

<sup>2</sup> Archives des maladies du cœur, Paris, June, 1913, vol. vi, No. 6.

unimpaired its influence on already established lesions. The hemorrhages stopped after two or three injections of the peptone, and they did not leave the patient so weak as before the peptone treatment. In six cases of purpura, peptone had a marked curative action in some, but it was less evident in others, especially in the more chronic cases.

Schreiber<sup>1</sup> made an intravenous injection of 200 e.e. of a 5 per cent. solution of *grape sugar* in a patient with severe hemorrhages from the stomach, and the hemorrhages did not recur. He had a similarly favorable experience in a case of intestinal hemorrhage in typhoid, and since then has applied this measure in a number of cases of internal hemorrhage from various causes. Kausch thus infuses up to 2000 c.c. of a 5 or 7 per cent. solution, but Schreiber has never injected over 200 c.c. of a 5 up to a 20 per cent. solution. No disturbances of any kind were observed by either Kausch or himself, and his patients did not develop glycosuria thereafter. Von den Velden ascribes the benefit to modification of the osmosis, the tissues being compelled to yield up to the body fluids substances which promote coagulation and thus reduce the tendency to hemorrhage. The result of an infusion of a hypertonic solution is a prompt hydremia and rise in the freezing-point of the blood, with increased diuresis. Von den Velden's research was made with hypertonic salt solution, but sugar deserves the preference over salt, as the sugar has a nourishing value which is useful for patients debilitated by severe hemorrhages. The sugar solution is better than serum for hemophiliacs as there does not seem to be any danger of inducing anaphylactic disturbances. In the one case of hemophilia in which Schrieber has tried it, the bleeding kept up the first day, but decreased the second day, and by the third day the hemorrhagic tendency seemed definitely arrested; in all preceding bleeding periods, the hemorrhages had kept up for a week, very severe. He adds that cane sugar seems to act the same as grape sugar and can be used instead of the latter.

**Scurvy.** No advance in our knowledge of scurvy has been reported in the literature of the year. The work of Hart, Holst and Frölich and Furst in experimental scurvy, and the report of Baumann and Howard on the metabolism of the disease, all reported in PROGRESSIVE MEDICINE (June, 1913, pp. 356, 357, and 358), are the latest contributions to the advance of our knowledge of this subject.

Hart's<sup>2</sup> experimental researches have established the identity of scorbutus in infants and adults. The bone changes are identical, but he warns that the diagnosis may be difficult when the classic symptoms are absent: bleeding of the gums, pains on motion, and swelling of the joint ends of the bones, generally in the leg, while the joints themselves are spared. Differentiation is scarcely possible when this classic triad

<sup>1</sup> Therapie der Gegenwart, May, 1913, vol. liv, No. 5.

<sup>2</sup> Centralbl. f. die Grenzgebiete der Med. u. Chir., September 8, 1913.

is not pronounced or is scarcely developed. Exophthalmos may be the only symptom, for a time, of infantile scorbustus; Habs had a case of this kind which he was unable to explain until the eyelids became discolored, like a "black eye." Small linear hemorrhages in the upper lid were evident in Hart's experiments on monkeys.

The sudden appearance of the swelling of bones is often a clue to the diagnosis. Special emphasis is laid on the warning never to incise one of these swellings; they retrogress soon and do not need incising, while the danger of infecting the subperiosteal hematoma is great. The hematoma may be very large; in one of Hart's monkeys the entire skull was capped by a subperiosteal hematoma. Hematuria may be the early and only sign of a hemophilic tendency, and it may occur with, or without, actual nephritis. Finkelstein has reported a case of fatal hemorrhagic nephritis in two brothers fed exclusively on sterilized milk, and he explained the clinical picture as a manifestation of scorbustus. The sensitiveness of the bones is an early sign of true scorbustus in young children; they draw up the legs on the abdomen at the slightest touch. The prompt subsidence of the fever when raw milk is given confirms anew the importance of dietetic treatment. Anatomic restitution is a very slow process, and cases are known of return of the symptoms of scorbustus. Finkelstein has reported recurrence after thirteen months of apparent recovery.

Prophylaxis is the main point, avoiding artificial and highly sterilized food for young infants from the very first. If they are absolutely necessary, the period of their use should be restricted to the minimum.

Fränkel described certain changes in the bones in infantile scorbustus which were revealed by Röntgenograms. These he considered characteristic and of diagnostic value. They may be found before any of the cardinal symptoms of the disease appear, and before there is any evidence of subperiosteal hemorrhage, either clinically or through the *x*-ray. The changes, as shown by the *x*-ray, consist of a definite "white line" ("Trummerfeld zone") in the negative at the end of the diaphysis and at the junction of the epiphysis and the diaphysis. Talbot, Dood and Peterson<sup>1</sup> have studied the occurrence of this "white line" with a view of establishing its value in diagnosis. In addition to their study of it in clinical cases, they have studied it in experimentally-produced scorbustus in guinea-pigs and monkeys, having practically repeated the experiments of Hart and Holst and Frölich for this purpose.

Their investigations have led to the conclusion that scorbustus may be produced experimentally in the guinea-pigs and in the monkey, and that the "white line" can likewise be produced in these animals. Under the microscope, this line appears as an area of increased density, and on the radiograph its presence is a constant sign in infantile scorbustus. It may persist many months after there is a complete clinical

<sup>1</sup> Boston Medical and Surgical Journal, August 14, 1913.

cure, which suggests that the pathological changes in the bones are not repaired for a long time and that this repair is very slow.

Glazer<sup>1</sup> reports two cases of scorbatus in school children. In both of these the *x-ray* findings were characteristic, well-defined white lines showing in the negatives. The second case occurred in a boy, aged six years, who had refused all food, excepting rolls and boiled milk. In a year after adopting this very restricted diet, scurvy developed in a severe form. Recovery, however, was rapid when raw milk and lemon juice were prescribed.

Meyer<sup>2</sup> relates three typical cases to show that when other causes for the non-thriving of infants can be excluded, the trouble may prove to be an unsuspected tendency to infantile scorbatus. This view is supported by Hart's experience<sup>3</sup> in the production of experimental scorbatus in monkeys. The improvement in these cases following a change of the milk, with the addition of a little fresh fruit or vegetables, confirms the assumption of an underlying tendency to scorbatus.

In summing up the symptoms of a case of Barlow's disease in an infant fed on pasteurized cow's milk, Pfender<sup>4</sup> says there was very slight anemia manifested by a moderate pallor of the conjunctiva and of the skin of the face. Pain, and a form of pseudoparalysis were present, but there was no enlargement of the bones. There was some hemorrhagic swelling and softening of the gums, but exophthalmus and hemorrhagic swelling of the eyelids were not present. No extravasation of blood into the skin or mucous membranes occurred. While there was no visible hematuria, erythrocytes were present in the urine. Fever was absent throughout the course of the disease. The author concludes that evidently a certain proportion of antiscorbutic properties still persisted and prevented the development of a severe typical case of scurvy.

de Sagher<sup>5</sup> has found that the increasing use of artificial foods seems to be increasing the prevalence of scorbatus in infants. He has encountered six well-defined cases during the last year, and describes eight in detail. They were all in well-to-do families, as the children of the poor are not fed on these expensive artificial foods and usually are given early a little food from the family table. He is convinced that incomplete forms of scorbatus are more frequent than is generally recognized; he knows of a number of instances in which the infants were treated for Pott's disease or coxalgia or osteomyelitis. Even Marfan diagnosed in one case "pseudoparalysis of syphilitic origin," which proved to be merely scorbatus. Hutinel warns that scorbatus should be thought

<sup>1</sup> Berl. klin. Woch., February 3, 1913.

<sup>2</sup> Therapie der Gegenwart, March, 1913.

<sup>3</sup> PROGRESSIVE MEDICINE, June, 1913, p. 357.

<sup>4</sup> Medical Record, New York, April 19, 1913.

<sup>5</sup> Annales de Médecine et Chirurgie Infantiles, March 15, 1913, vol. xvii, No. 6.

of first in every case of painful paraplegia in an infant, or even when the child is merely a little uneasy when its legs are touched. Do not wait for further symptoms of scorbustus to develop. Scorbustus is exceptional under five months and after two years of age. In de Sagher's cases, some of the infants had been fed on condensed milk, some on nutricia milk, some on maltosan, and some on boiled milk. To ward off any danger from this cause, he orders systematically, after the age of six months, from 2 to 6 teaspoonfuls a day of grape juice, adding to this after two or three months from 1 to 3 teaspoonfuls of some preserve, his preference being banana jam. This not only wards off scorbustus, but it combats constipation and supplies a little iron. Scorbustus has never developed among the children fed in this way.

The description of two unusual cases of infantile scurvy has been contributed by Pritchard<sup>1</sup>. The interest in the first case lies in the extensive development of edema from which no part of the body seemed exempt. The infant, aged nine months, had a pallid, waxy appearance. Another peculiarity of the edema was that, although it looked as if it would easily pit on pressure, it was practically impossible to obtain a permanent indentation with the fingers, no matter how deeply they were inserted into the skin. The second case was as follows: On March 30, an infant, aged ten months, fell from a mail cart on to a mat on the floor; it did not appear at the time to be seriously injured, but the same evening a swelling gradually appeared on the side of the head on which it had fallen. On the following day, examination was negative. A few days later the swelling had increased rather than decreased in size, and the child seemed lethargic and disinclined to move. On examination, Pritchard could find no evidence of cerebral pressure, but, on inquiry, he discovered that the infant had not been well for some days before the accident. The child had been lethargic, disinclined to move, had had no appetite and seemed generally indisposed. The method of feeding again was not without its significance. There was general tenderness over all the limbs, and evidently strong aversion to being moved or otherwise disturbed. The gums were spongy and of a purple color. Pritchard therefore prescribed an antiscorbutic diet of orange juice, raw-meat juice, egg-water and milk, and strongly advised against aspiration or other interference with the hematoma of the scalp, which, by the time of examination, had assumed an enormous size. The general condition of the infant rapidly improved under this treatment, and at the end of ten days it had practically returned to normal health and showed an increase in weight of over 18 ounces.

### GOUT.

The work of the year on gout has consisted largely of the description of methods for the quantitative determination of uric acid in the blood

<sup>1</sup> *Lancet*, London, June 7, 1913, vol. i, No. 4684.

and of studies on the effects of drugs and diet on the disease. In addition, there have been some observations made on the metabolism of gout.

A rather novel method for the determination of uric acid in minimum quantities of blood-serum and other body fluids has been devised by Roethlisberger.<sup>1</sup> A small quantity of blood is drawn from the finger tip or the lobe of the ear into a special glass tube, from 10 to 15 drops being usually sufficient for from six to nine tests, which are made simultaneously and serve to control one another. The glass tube must be kept in an upright position for several hours, until complete separation of the serum has taken place. If necessary—especially if placed in an even temperature—the blood may be kept from twelve to twenty-four hours. If kept for a longer period of time there will be loss of uric acid by fermentation or putrefaction.

The best environment for the test is a dark room with a red light, though equally good results may be obtained in a room with a subdued light, or one lighted by a small electric bulb placed at a distance of two or three yards. Two, three, or more strips of the reagent paper—a special kind of filtering paper impregnated with nitrate of silver—are placed on a glass slide. The silver paper should not be exposed to the light except during the time necessary for manipulations; in the intervals it must be screened. With a dropper, 15 per cent. solution of carbonate of soda is dropped on the paper, allowing a certain margin to surround each drop. The drops must be very small and must absorb quickly, leaving a perceptible round spot. After waiting two or three minutes, a quantity of the blood-serum is withdrawn by a dropper from the glass tube containing the blood; it is dropped slowly on the round spots made by the carbonate on the test papers. In two or three minutes more the strips of paper are lifted from the glass slide and placed to soak in a porcelain or earthenware dish filled with water. The nitrate of silver now dissolves, while the carbonate remains insoluble. The basin must be kept covered to protect the strips of paper from the light until the nitrate is totally dissolved, which generally requires at least thirty minutes. They may be left to soak much longer without harm. The strips are now ready for fixation. They should be removed from the basin and placed in a solution of ammonia (one part of pure ammonia to four parts of water), which removes any un-reduced carbonate of silver. Five minutes are sufficient for this process. The strips of paper are then placed in clean water screened from the light, to wash them thoroughly and to remove the ammonia and remains of the salts of silver. After remaining for several hours in the water, the strips are dried between blotting- or writing-paper, care being taken to protect them from the light. The dried strips are then ready to be placed under the scale; a color scale is necessary for the determination. By comparing the

<sup>1</sup> Medical Record, November 1, 1913.

color and the intensity, the degree of reaction and the proportion of uric acid contained in the blood can be determined. Only spots with distinct outline are to be considered.

A method is described by Ziegler<sup>1</sup> which, he claims, does away with many of the disadvantages of other methods, such as the disturbing presence of residual nitrogen and the error-loss of uric acid through its absorption by coagulated albumin. The technique follows the principle of the Kruger-Schmidt method based on the fact that copper sulphate forms an insoluble combination with uric acid and urates. This occurs with complete precipitation of the urates, even when enough sodium hydroxide has been added to the fluid to keep the albumin in the serum from precipitation as the mixture is boiled and evaporated down to a third of its bulk. After this evaporation, the mixture is centrifuged until the fluid is limpid. The sediment is then treated with sulphuric acid which at once dissolves the copper urate compound and the uric acid thus liberated is titrated against potassium permanganate. The test reveals uric acid down to 0.005 or 0.025 gm. in 10 c.c. of serum.

The method recently described by Folin and Macallum for the colorimetric determination of uric acid in the urine has been found to be not directly applicable to all kinds of urine. For instance, that of certain animals as the rat and cat and also certain kinds of pathological human urine, those containing albumin or sugar where on evaporation coatings of inert materials make it impossible to remove the interfering polyphenol compounds. Hence a procedure has been devised by Folin and Denis.<sup>2</sup> The method is carried out as follows:

From 1 to 2 e.e. of urine are measured into an ordinary centrifuge tube by means of a modified Ostwald pipette. A sufficient amount of distilled water is then added to bring the volume of the liquid in the tube to about 5 e.e., six drops of 3 per cent. silver lactate solution, two drops of magnesia mixture, and a sufficient amount (10 to 20 drops) of concentrated ammonium hydrate to dissolve the silver chloride are then added. The tube is now centrifuged for one or two minutes, the supernatant liquid poured off and to the residue in the bottom of the tube are added five or six drops of freshly prepared saturated hydrogen sulphide water and one drop of concentrated hydrochloric acid, and the tube is placed in a beaker of boiling water until all excess of hydrogen sulphide has been driven off.

As hydrogen sulphide gives a blue color with the "uric acid reagent," care must be taken to obtain its complete removal. To determine whether this has been accomplished, one drop of 0.5 per cent. lead acetate solution should be added to the contents of the tube after the latter has remained in the water bath for about five minutes, and, if any hydrogen sulphide still remains, a dark brown precipitate will be

<sup>1</sup> Münch. med. Woch., May 20, 1913.

<sup>2</sup> Journal Biological Chemistry, 1913, vol. xiv.

formed. If this condition be obtained, the tube should be returned to the water bath for a further period of heating.

When the tube has been cooled, add 2 c.c. of the uric acid reagent, 10 c.c. of saturated sodium carbonate solution, transfer to a 50 c.c. volumetric flask and make up to volume. The color comparison is then made in the usual manner against the color obtained from 5 c.c. of the standardized uric acid-formaldehyde solution (or a freshly prepared pure uric acid solution).

An elaborate study of oversaturated solutions of uric acid and its salts has been made by Kohler.<sup>1</sup> In this work he has demonstrated, by means of dialysis and electric conductivity, that in hyperconcentrated solutions of sodium urate we are not dealing with a colloidal but with a true oversaturated solution. Small amounts of colloid could be demonstrated only in those saturated and supersaturated solutions which showed a slight opalescence. The boundary between the metastable and labile states of a pure solution of sodium urate at 37° occurs at about two and a half times oversaturation. Crystallization is not immediately or suddenly brought about by the further addition of sodium urate as in other oversaturated solutions after inoculation, but the solution equilibrium is lost slowly, and the rapidity of this loss depends upon the amount of original substance added. From this, it is to be inferred that the greater the concentration of the solution, the more rapidly oversaturated solutions in the labile sphere attain equilibrium.

In the presence of sodium chloride, the boundary of the metastable state is relatively higher. In a five times oversaturated solution containing 1 per cent. of sodium chloride, no spontaneous crystallization takes place. Pure uric acid forms oversaturated solutions, but here the further addition of the substance promotes rapid crystallization. Uric acid has practically no metastable state, for, in slightly oversaturated solutions, after a short time spontaneous crystallization takes place. Equilibrium is lost much more rapidly and easily. The equilibrium of uric acid urate does not occur, or occurs very slowly under the influence of a weakly acid reaction upon urate in solution. The importance of these results for physiology and especially for the solution relations in the urine is that we are dealing with a true oversaturated urate solution from which uric acid is not set free through the usually weak acid reaction; since manifestly, there is no less of equilibrium whereby solution conditions are rendered more favorable.

Ehrmann and Wolff,<sup>2</sup> in their researches on the blood serum of gouty individuals, have determined that uric acid in determinable quantities may be present in the blood-serum of normal individuals on a purin-free diet, and that, in cases of typical gout on a purin-free diet, the uric

<sup>1</sup> Zeit. f. klin. Med., 1913, vol. lxxviii.

<sup>2</sup> Münch. med. Woch., 1913, No. 38.

acid content of the blood-serum may be less even than that of normal individuals on a purin-free diet. Hence, they have found no characteristics in the blood-serum of their cases of atypical gout. Some hours after the administration of atophan they found that the uric acid in the blood-serum usually showed no change. In one case, however, it was not determined. The urea and purin bases showed no notable change. Contrary to the findings in the whole blood in which, according to Wieehowski, the content of the purin bases is four to ten times greater than that of uric acid, in the serum the uric acid almost throughout is distinctly greater than the content of purin bases. The H-ion concentration of the blood of gouty individuals is, in many cases, distinctly higher than that of normal individuals, and even than that of diabetics with comatose or precomatose symptoms. This points undoubtedly to the occurrence of a lessened alkalinity of the blood in gout. The blood-serum of gouty individuals in some cases presents a lipemic appearance.

Skorczewski and Sohn<sup>1</sup> have studied the metabolism of gout under the influence of *radium therapy*. They conclude that under this treatment the end balance of metabolism, as expressed in the taking on of body weight, is not injured in the least. An increased diuresis was observed in 5 of 6 cases. The treatment exerted no influence upon protein destruction in the organism. In four patients, on the fourth and fifth radium days, changes were observed, in the form of an increase in the excretion of nitrogen, uric acid and mineral and neutral sulphur. In 2 of the cases, this influence was shown only in the uric acid and the neutral sulphur. Excepting in these instances in the early radium days there was no apparent change in the output of neutral sulphur. The excretion of uric acid in four other cases went hand in hand with the excretion of the neutral sulphur. If atophan and sodium "nucleinicum" are administered, excretion of uric acid and neutral sulphur is greater in the radium period than in the period preceding. The authors conclude from this that radium exerts an influence on the organism through a reduction of its power of oxidation.

Haskins<sup>2</sup> has carried out experiments on 21 students to determine the effect of atophan and novatophan on endogenous uric acid excretion of normal men. The students were placed on a purin-free diet for one week before the drugs were administered. The authors conclude, from these experiments, that atophan is slightly more effective than novatophan, and that the main effect of both drugs is probably a draining of uric acid from the blood, leaving the uric acid content of the latter subnormal.

Folin and Lyman<sup>3</sup> conducted eight experiments to determine the effect of atophan on the uric acid content of the blood. In six of these

<sup>1</sup> Zeit. f. exp. Path. u. Therap., 1913, Heft 1, vol. xiv.

<sup>2</sup> Journal Pharmacology and Experimental Therapeutics, September, 1913.

<sup>3</sup> Ibid., July, 1913.

experiments, patients suffering from gout were studied. The administration of the drug in every case led to an increase in the uric acid elimination and to a marked reduction of the uric acid in the blood. The increased output therefore represents the elimination of uric acid which had previously accumulated in the blood, and the previous accumulation represents a corresponding kidney inefficiency. In the absence of any other reasonable explanation, such independent variations in the accumulation of different products in the blood must be explained on the basis of a selective activity on the part of the kidney and corresponding to such a selective activity a partial and selective deterioration.

A contrary view is expressed by Retzlaff<sup>1</sup> who says that the action of atophan is not to be looked upon as a selective kidney action, but rather as a direct influence on purin metabolism. This latter expresses itself in an increased cleavage of uric-acid-forming substances brought about by an increase of fermentative processes in the metabolism of nuclein through the action of atophan.

Graham and Poulton<sup>2</sup> found that the consumption of a diet consisting of protein and fat of sufficient caloric value causes a fall in the endogenous uric acid output of between 30 and 50 per cent. If most of the fat in the previous diet is replaced by carbohydrate, there is no fall in the output of endogenous uric acid. A fall in the endogenous uric acid is also produced in two other conditions: (a) starvation during the first few days; (b) the consumption of a carbohydrate and fat diet. The following possible causes to account for the diminution in the uric acid output have been considered by the authors: (a) diminution in protein metabolism; (b) loss of body protein; (c) acidosis; (d) increased fat metabolism; (e) the interaction of protein and carbohydrate metabolism. Decided objections are raised to the first four hypotheses, but the last hypothesis seems to agree with the facts observed by other authors as well as Graham and Poulton.

Minkowski<sup>3</sup> warns that recent research has demonstrated that uric acid can be found in the blood in normal conditions, even on a diet free from purins. The mere discovery of uric acid in the blood on a purin-free diet does not necessarily mean gout. The proportion is much larger in those inclined to gout. This accumulation of uric acid is not due to simple exaggeration of the production of uric acid; when this occurs, there is always a larger uric acid output in the urine. In gout, the urine does not contain an abnormal proportion of uric acid, and it seems as if the endogenous production of uric acid was rather below normal than above. The trouble seems to be retention, and the question is why the abnormally large proportion of uric acid in the blood is not passed out through the kidneys. The kidneys seem to become

<sup>1</sup> Zeit. f. exper. Path. u. Therap., 1913, vol. xii, Heft 2.

<sup>2</sup> Quarterly Journal Medicine, London, October, 1913, vol. vii, No. 25.

<sup>3</sup> Men. Klinik, May 18, 1913, vol. ix, No. 20.

impermeable for uric acid alone; gout is not uremia. The assumption seems inevitable that either the uric acid itself has become modified in its physical or chemical properties, or else certain metabolic processes which govern the fate of the uric acid have become modified—the trouble does not seem to be in the kidneys themselves. Treatment should therefore aim to reduce all the metabolic processes in general to a lower plane, and thus in this way act attenuatingly on the metabolic process assumed to be responsible for the gout. This should be supplemented by excluding from the diet the purin bodies which have been recognized as the source of gout. He says that the purins in coffee, tea, and cocoa are in a methyl compound which does not become transformed into uric acid. These beverages may at most increase transiently the uric acid content of the urine by their diuretic action, thus sweeping out a certain amount of the previously retained uric acid. There is no reason for prohibiting these beverages in gout solely from the stand-point of uric acid. Boiled meat contains less purin bodies than roast, but fish does not differ materially from meat, in general, in this respect. Small fish contain more purins than beef and pork. In conclusion, he calls attention to the fact that proteins form what may be called an acid diet, that is, an-ions (sulphuric acid and phosphoric acid) are generated among the resulting products, while vegetables constitute more an alkaline, a kat-ion, diet, and these facts are not without influence in the management of gout.

Garrod<sup>1</sup> declares that the greatest progress in the dietetic treatment of gout in recent years is the recognition of the important part played by uric acid in metabolism and the discovery that a diet can be arranged which is almost free from purins and yet contains plenty of albumin; milk, eggs, and cheese are particularly useful on this account. But he emphasizes that the diet is not everything in the management of gout; moderation in all things, not merely in eating and drinking, is the golden rule by which the gouty are kept free from attacks. Avoidance of fatigue, and of even the slightest trauma, and everything liable to upset the precarious balance is the key to success. He had a patient develop an attack after mere removal of ear wax; another has an attack whenever he takes a long railroad ride.

Le Gendre,<sup>2</sup> in a paper on the dietetic treatment of gout, divides the patients suffering from this disease into three principal classes according to the symptoms which precede gout of the joints or which alternate with it. (1) Those who show in the main digestive disturbances; (2) those with circulatory and nephritic changes; (3) those with predominating nervous disturbances. He differentiates between the diet during the attacks and that between the attacks. In the former, he lays stress upon the taking of liquids, about 3 liters per diem, and upon an extreme limitation of solid food. Between the attacks, he gives, to those patients

<sup>1</sup> Med. Klinik, July 20, vol. ix, No. 29.

<sup>2</sup> Ibid., 1913, No. 43.

of the gastrohepatic and pancreatico-intestinal group, a scanty diet poor in purins which contains little meat, simple cooking, and a small amount of fermented drinks; above all, a diet which will encourage the best possible function of the different digestive organs and lay the least stress upon them. For the angionephritic patients, he recommends a diet without meats, poor in purins, without alcohol, and either free from, or poor in, chlorin, consisting principally of milk, eggs, and vegetables. The dietetic procedure with those patients of the nervous class is the administration of a mixed diet with absolute prohibition of alcohol and all stimulants.

### DIABETES.

The writings of the year on diabetes have been numerous, but it can hardly be said that our view-points regarding pathogenesis and treatment of the disease have undergone any definite change. Some new experimental facts have been ascertained and some excellent work has appeared on the general metabolism in this condition. Perhaps the most fruitful field which has been opened up is the study of the blood with respect to its sugar content.

**Pathogenesis.**—A very lucid presentation of the sugar mobilization theory of diabetes, along with a discussion of the principles of treatment in this disease, is given by von Noorden.<sup>1</sup> Diagrammatically, and in the text, he represents the liver as the sugar factory and store-house. On the one side stands the intestine, which supplies the sugar, and on the other, the tissues which demand it. On the one hand, the chromaffin system stimulates production in the factory, while, on the other, the pancreas inhibits this production. As accessory factors on the one side, the central nervous system stimulates the chromaffin system, and thus, indirectly, stimulates activity in the liver. On the other side, the thyroid gland and hypophysis stimulate liver activity by inhibiting the inhibitory influence of the pancreas, while the parathyroid glands inhibit liver activity by stimulating the inhibitory influence of the pancreas. From these considerations we are led to the conclusion that the excretion of sugar in the urine is not indicative of one disease alone. Of course, under all circumstances, glycosuria is a sign of increased production of sugar, and of an excess of sugar in the blood stream. The cause of the disturbance may be found in various places, but in the case of renal diabetes, several sources are of unequal importance: (1) Primary disease of the liver itself. This plays a subordinate role. Glycosuria in this condition is the exception, and not the rule. (2) An anomalous demand on the part of the tissues for more sugar than they actually need. This is theoretically possible, and undoubtedly plays a part in phloridzin diabetes, but has extremely

<sup>1</sup> American Journal of the Medical Sciences, January, 1913.

doubtful, if any, connection with human diabetes. (3) The intestines may supply too much sugar for the glycogen function of the liver to take care of, and the untransformed sugar passes into the blood (transitory alimentary glycosuria). Should sugar appear in the urine of an adult upon an average sugar and starch diet, it would be wrong to regard it as a physiologic or harmless glycosuria. It should be considered an indication of disturbed sugar metabolism, a slight form of diabetes. The term "alimentary glycosuria" has led to regrettable and costly errors. (4) Anomalies of stimulation from the chromaffin system, which may occur from disease of the suprarenal itself, or from disturbances in the central nervous system, or in the path connecting this with the suprarenals. These influences are likely to be transitory. (5) Anomalies of the influence of the pancreas are by far the most important in human diabetes. These may be due to disease of the pancreas itself, or to the influences exerted by the thyroid, hypophysis, or parathyroids.

These conditions emphasize the view that diabetes is a complicated disease, and show how little aid can be rendered to the patient if the attention is focussed on the glycosuria alone. The condition demands that the functional powers of all the organs of the body be considered. Each case is a law unto itself, and marked variations from a common type often occur.

However, no matter where the primary disturbance is localized, or whether one or more of the controlling factors are acting abnormally, in diabetes there is always present an enormous irritability of the sugar-forming apparatus of the liver; normal impulses are responded to, not with an ordinary output of the required sugar, but with an extraordinary, almost unlimited, sugar production. This lack of coördination between the intensity of stimulus and extent of response is the characteristic feature of the disturbances of metabolism in diabetes. Naturally, there are considerable gradations; at one end the hypersensitiveness of the sugar-forming apparatus is only slight, and is only revealed when the overstraining is specially intense; at the other end, the hypersensitivity manifests itself even to the slightest stimuli. In fact, it is the extent of difference between stimulus and response which determines the severity of the diabetic process.

All the stimuli which experimental investigation has shown to act as irritants to sugar production exert an increased influence in diabetes: such as the in-streaming of carbohydrates and the digestive products of proteins into the liver; acceleration of general metabolic processes by excessive and tiring muscular work or acute febrile attacks; psychical and other nervous excitations; injections of adrenalin; thyroid gland feeding, etc. There is urgent need to calm the excessive irritability of the sugar mechanism. Every unnecessary burden must be avoided. If we are able, by a wise choice of food and the exclusion of other

irritants, to lower the demands upon the sugar factories, the sugar production in slight cases will keep within normal limits, almost without exception, and the glycosuria will disappear.

As a rule, the patient does not fully avoid the excessive overloading; there follows a marked irritation of the sugar mechanism; the urine may even still not show sugar to an ordinary analysis, but every such transitory stimulation increases the sensibility of the organs in the future. The more frequently this overloading is repeated, the greater will be the difference between the strength of stimuli and the amount of response. Bread, and other meal foods, which were taken well at first, later lead to glycosuria, or, in other words, a slight diabetes shows definite progression. In addition, other disturbances arise, chief of all the formation of acetone and associated substances. This relates to anomalies of the metabolism of fat. Normally, the fat of the tissues is burned to carbon dioxide and water. The presence of carbohydrates (particularly glycogen) is necessary for the cleavage of fat to follow its proper course. It is evident, therefore, that the increase of carbohydrates in the food will deal with acetone formation by providing the necessary amount of protective carbohydrates. The worst cases excluded, this certainly leads to the desired end; but it has proved a dangerous type of therapy. The additional carbohydrates constitute an exceedingly strong excitor of the sugar mechanism and damage its regulation more and more. The way to combat the process is to protect the sugar mechanism by sparing its work—by systematic diminution of the carbohydrates as well as of the irritating protein material. Then the excited sugar formation and the acetone bodies decrease. To a certain degree, acetone formation in diabetes is not at all dangerous. When treated properly, it is easier to deal with the acetonuria than is generally supposed.

Since the altered relations between the intensity of the stimulus and the extent of the response show considerable gradations, we may assume that the means of treatment will also call for manifold variation. As a matter of fact, practically all the therapeutic methods find an application in diabetes. The chief excitor among the foodstuffs is the carbohydrate, and its restriction, for more than a hundred years, after many aberrations, has always constituted the most prominent factor of diabetic therapy.

For a certain number of diabetics 80 plus 100 grams of carbohydrates per day is the proper amount, that is to say, the quantity with which the urine remains free from sugar. For the greater number of patients, however, this quantity is not suitable. It may be too high or much too high; or it may be too low or much too low. In both instances the result will be a damage to the tissues. If more carbohydrates are consumed than the liver can utilize in an ordinary fashion, the diabetic disturbances of metabolism increase more and more, in one case slowly, in another rapidly, but in all there is a persistent increase.

After the carbohydrates, there are the proteins to consider as irritants of the sugar mechanism. They pass direct to the liver and there undergo a further cleavage. By this means substances are produced which are transformed easily into sugar. The proteins are, therefore, to be regarded as sources of sugar, although the yield is not great; in fact, it is probably much less than the physiologist assumes. On the other hand, however, the proteins are powerful excitants of the liver cells, and are able to induce marked activity of the sugar-producing centres; in the healthy individual, whose sugar production is strictly controlled by the regulating organs, this excess of activity does not result. In diabetics, however, in whom the regulating apparatus is abnormal the response to these excitants is considerable.

The third important foodstuff—fat—does not exert any direct irritant action upon the sugar production. Fat, of course, is a source of sugar, but it plays a passive part, and is thus not comparable with the active powers of the carbohydrates and proteins; it is only used by the liver cells when other material is not at hand. Under conditions of marked excitation of the sugar mechanism, large quantities of fat are utilized and sacrificed. This explains the emaciation which comes on in severe cases of diabetes.

Alcohol is another material which acts as a food and does not irritate the sugar-forming process. On the contrary, it appears to diminish the formation of sugar.

In discussing the theories of diabetes, Minkowski<sup>1</sup> says, in the first place, concentration of the attention upon the catch words, "disturbed utilization," or "increased formation," gives no proper idea of the differences between the two theories. One cannot deny that a temporary elimination of sugar may be brought about by an overflooding of the organism with sugar, as in certain cases of alimentary glycosuria, or through a sudden outpouring of sugar from the glycogen repositories as in the case of *la pique*, and as probably also takes place in adrenalin glycosuria. Furthermore, those who consider that the disturbed utilization of sugar is the principal factor in the origin of diabetes do not deny that the production of sugar may be increased in the organism. The body which is not able to oxidize sugar is in a condition of carbohydrate hunger, notwithstanding the fact that its fluids are overladen with sugar. The circulator mechanisms which normally coördinate sugar production with sugar requirement are consequently continually stimulated. If, therefore, it should be proved that the production of sugar is greater than normal, this does not prove that the increased sugar formation is the cause of the glycosuria. It could just as well be the result of the disturbed utilization of sugar. The question is this: Can it be proved that the diabetic organism has the power of the normal organism to utilize sugar, whether that sugar be

<sup>1</sup> Medical Record, February 1, 1913; translation by Lusk.

ingested or be produced within the organism itself? The newer views maintain that this is the case. It seems to me that the proof has not been offered. It is true that most diabetics can utilize certain quantities of carbohydrate, and such utilization may increase when increased quantities are given; but, one must recollect that human diabetes depends upon the reduction and not the complete abolition of a function, and that the powers of even a diseased organism may be partially increased when increased demands are made upon them. The idea that the utilization of sugar is not disturbed in diabetes must, of course, present great difficulties to the clinician. It appears to me that a "quantitative mental error" is here involved. How is one to imagine a continuous glycosuria of the intensity found in human diabetes, or even in experimental diabetes, without any disturbance of sugar utilization, and occurring only as the result of an increased sugar production? In the last analysis, it can happen only through a delay in the mobilization of sugar. For even in the normal organism deposited carbohydrates are sooner or later converted into sugar and oxidized as such. Even though it is possible to conceive that an overflooding of the organism with sugar and consequent glycosuria may be brought about through the discharge of accumulated glycogen stores, as in the case of *la pique*, how can it be possible that after the exhaustion of these reserves and during starvation, a prolonged and continuous sugar elimination takes place as the result of the overproduction of sugar when the sugar utilization is not at all disturbed?

In these days, however, when one again speaks of "diatheses" and pays attention to the patient's "constitution," the question is asked, Is there a specific locality to which the diabetic disturbance may be attributed? Is not the disease rather a "constitutional anomaly," a "disease of metabolism," instead of being a localized disease of an organ?

The term "general disturbance of metabolism" is nothing but an aid for the description of disturbances which have not as yet been localized. The more profoundly one understands the processes of metabolism, the more firmly convinced must one become that, in the higher animals at least, the separate phases of the metabolic processes are sharply localized.

We hardly know anything of the "general metabolism" of protoplasm. Whenever a disturbance of very definite order occurs, such as that in diabetes mellitus, there is every reason to seek for a localization of this disturbance. "Diathesis" should not again be permitted to become a word to be used where comprehension fails. The cause of the production of diabetes and the controlling factors thereof include almost numberless possibilities, which may explain the many variations which present themselves clinically. The supporters of these doctrines do not deny that in far the greater number of the cases the dominant

role is played by the pancreas. But they ascribe to this organ merely the importance of a brake, whose removal results in the unhindered activity of adrenalin. I certainly do not deny that other organs may contribute to regulate carbohydrate metabolism and, therefore, may have an influence upon diabetes. Without further proof, it ought not to be concluded that one organ acts upon another, just because the end-result of the action of one organ may be increased or decreased by the co-activity of another organ. It is just as though one argued that since a fortune may be accumulated by increasing the income or by diminishing the expense account, therefore an increased income must decrease expenses, and *vice versa*.

Without prejudice to the idea of the highly probable nervous and chemical correlations existing between the various organs, one may still consider that the influence upon the organism caused by a functioning organ or by a lesion of that organ, is much more probably due to the fact that each organ has a certain positive and, for itself, specific functional obligation. In this sense the adrenals may contribute directly or indirectly to the mobilization of sugar; the thyroids may cause only an increase in protein metabolism, although they may also act in other ways to increase sugar formation. As far as the pancreas is concerned, I would, both upon experimental and clinical grounds, attribute to it a pronounced influence upon the oxidation of carbohydrate in the organism. If we today treat diabetes by diminishing the carbohydrate intake, it is because we endeavor in that way not only to cause sugar to disappear from the urine, but also to spare from activity a disturbed function, and thereby cause its entire, or, at least, its partial recuperation. Von Noorden does, in fact, state that even under the new doctrines, the tried and tested method of limiting carbohydrate ingestion, the "sparing therapy," still holds, because, he says, sugar, of all other substances, stimulates to the greatest glycogen production, "acts as a whip to the involved organs." But, strictly considered, this is perhaps not quite logical. One might argue that if the utilization of sugar be not disturbed in diabetes then perhaps there ought to be some replenishment of the sugars lost to the organism, so that its capacity for work should be maintained; and that the more carbohydrate given in the food the smaller would be the amount of sugar necessary to be built out of the valuable protein. In this way it could readily come about that dietary formulæ might be prescribed, as was formerly done, so that the more carbohydrate a diabetic excreted the more he should be given in his food.

Cohn<sup>1</sup> presents evidence to show that in diabetes the salt metabolism is abnormal, in that there is a deficiency in sodium and an excess of potassium. The cause of this disturbance is defective functioning on the part of the glands, the pancreas in particular, which are accumulators

<sup>1</sup> Deutsch. med. Woch., October 2, xxxix, No. 40.

of potassium. Treatment should aim to restore the normal balance between these elements. This has been empirically done by giving oatmeal to diabetics. Oatmeal ash contains 4.30 per cent. sodium to 23.73 per cent. potassium, while wheat flour has respectively 0.76 and 34.43 per cent., and rye flour 1.75 and 38.44 per cent. The proportion of sodium to potassium in oatmeal is thus 1 to 5.5 while with wheat flour it is 1 to 45—a difference enough to explain the benefit derived from oatmeal in diabetes.

Cohn has previously presented evidence to the effect that an important contributing factor in gout is likewise a disturbance in the metabolism of sodium and potassium. In gout, however, it is the sodium proportion that is abnormally large and the potassium abnormally low—just the reverse of what the author has found to obtain in diabetes. The organ in charge of the reserves of potassium, the pancreas, has become functionally incompetent, and potassium should be systematically administered. Among the facts he cites to sustain this theory is his finding that the blood in the pancreatic artery, just entering the pancreas, contained an average of 0.108 per cent. sodium to 0.014 potassium; the blood in the pancreatic vein, on the other hand, just emerging from the pancreas, contained only 0.094 per cent. sodium to 0.027 per cent. potassium.

To the objection that the total proportion of the salt in the body is so small as to be negligible, he replies that recent research has demonstrated the unsuspected importance of even minute proportions of certain cell constituents—even a single ion may in some circumstances decide the life or death of the cell. He enumerates, as follows, the points which speak in favor of the assumption that the diabetic is suffering from an excess of potassium and lack of sodium: (1) the frequent occurrence of free uric acid in the urine; (2) Rumpf and Dennstedt's finding of 0.2 sodium to 4.1 potassium in the ash of a diabetic's liver when normally both are about 1.5; similar findings were encountered in numbers of others; (3) accelerated ferment activity of the pancreas enzyme in contact with potassium salts; (4) the close resemblance between the symptoms of potassium poisoning and those of diabetes, especially the development of glycosuria after augmented intake of sodium; (5) increased potassium content of the urine in diabetics; (6) the resemblance between diabetic coma and the heart failure in potassium poisoning, and (7) Loewi's recent experiments with animals rendered diabetic showing that the diabetic heart muscle is extraordinarily sensitive to potassium. Cohn says, in conclusion, that his encouraging clinical experience with treatment on this basis has also confirmed the correctness of his premises.

Rodriguez<sup>1</sup> believes that one of the important factors in the etiology of diabetes is an excess of chlorides in the diet. The beneficial effect

<sup>1</sup> Revue de Médecine, February, 1913.

derived from a potato diet, which furnishes more than 350 grams of glucose, he claims is dependent upon the fact that the salts of potassium contained in the potato bring about the elimination of the retained sodium chloride as the potassium salt. The author has successfully treated six patients on a salt-free diet which was moderately rich in carbohydrates. This view seems diametrically opposed to that of Cohn.<sup>1</sup>

Dietrich<sup>2</sup> calls attention to the relationship which exists between gastro-intestinal disease and diabetes. Of 40 cases of diabetes studied, only 25 per cent. showed normal conditions in the gastro-intestinal tract; while 67.5 per cent. showed marked gastric catarrh or achlorhydria. In 3, out of 9 cases of diabetes, in which lavage was used without enforcing an antidiabetic diet, the glycosuria completely disappeared. The author is convinced that the gastro-intestinal trouble can be transmitted to the pancreas, and that, in all cases of diabetes, there should be a careful examination of the gastro-intestinal tract with the view of removing any abnormal conditions, thereby improving the pancreatic conditions which, in turn, will benefit the diabetes.

Castaigne<sup>3</sup> discusses diabetes of hepatic origin, and cites two cases. Acknowledging the difficulty of recognizing the liver as particularly responsible in these conditions, he recommends as a test that we instruct the patient to take only two meals a day, one at 11 A.M., the other at 6 P.M. The urine is then collected every two hours (this is of the greatest importance) and analyzed. In diabetics whose livers are deficient, the sugar is generally eliminated in its entirety only after a meal, the glycosuria being almost entirely alimentary. Between meals, little or no sugar will be found. When diabetes *post cibum* is found, it is an argument in favor of glycosuria depending upon imperfect working of the liver; all the more so, seeing that, at the same time, we find other classical signs associated with defective liver function. The diagnosis is confirmed when the glycosuria is found to disappear under the influence of substances which tend to stimulate the liver function (alkalies, liver extract, and preparations of iron); whereas, it becomes more pronounced when arsenic, which hinders the liver function, is given.

**Pathology.**—From a histological study of the pancreas, Koch<sup>4</sup> is led to the conclusion that the islands of Langerhans are not independent structures. True transition forms between the island cells and the tubule cells often occur. The islands do not possess a true capsule. Where this appears to be present, it has no more significance than other interlobular connective tissue. The islands of Langerhans arise mainly from the tubules and are to be looked upon as involution structures

<sup>1</sup> Loc. cit.

<sup>2</sup> St. Petersburger med. Zeitsch., November 12, 1913.

<sup>3</sup> Medical Press and Circular, June 11, 1913.

<sup>4</sup> Virchows Archiv, March, 1913.

of apparently non-functioning and non-functionable parts of the parenchyma. It is doubtful if they can be considered as "reserve material."

Aron<sup>1</sup> believes that the frequent occurrence of arteriosclerosis in diabetics can be explained by the fact that in this disease in consequence of a too rich nourishment or diet, a stretching or distention of the circulation takes place which favors the development of arteriosclerosis.

**Sugar Content of the Blood.** Research in diabetic conditions has been facilitated by the discovery of easily applicable methods for the determination of the sugar content in small amounts of blood. A method devised by Bang<sup>2</sup> requires only two or three drops of blood for the determination. These are taken directly from the lobe of the ear on a piece of good blotting paper 16 by 28 mm. The scrap of paper is held with forceps, and it is not allowed to soak up too much blood. It is then placed in a test-tube. A second test-tube holding 5 c.c. of a mixture of 136 c.c. of saturated solution of potassium chloride, 64 c.c. water, and 0.15 c.c. of a 25 per cent. solution of hydrochloric acid is heated, and when it boils it is poured carefully over the blood-paper. In order to have the fluid come in contact with all the blood, he holds the tube slanting. When entirely cool, not until after half an hour, the fluid is then poured into a third test-tube, and to it are added 5 drops of the Fehling I reagent and two drops of Fehling II. It is then boiled for half a minute and watched for two minutes. If no oxydul precipitates out in two minutes, the proportion of the sugar in the blood is below 0.15, that is, it is within practically normal range. The amount of oxydul thrown down is an index of the percentage of sugar in the blood as shown in the following table:

| Sugar solution<br>1 pro mille. | Salt<br>solution. | Fehling I. | Fehling II. |              |
|--------------------------------|-------------------|------------|-------------|--------------|
| 0.10 +                         | 5 c.c. +          | 5 drops +  | 2 drops =   | 0            |
| 0.15 +                         | 5 c.c. +          | 5 drops +  | 2 drops =   | + very weak. |
| 0.20 +                         | 5 c.c. +          | 5 drops +  | 2 drops =   | ++ distinct. |
| 0.30 +                         | 5 c.c. +          | 5 drops +  | 2 drops =   | +++ marked.  |

Bing and Jacobson<sup>3</sup> have studied the blood-sugar content by means of the Bang method. In normal individuals they found an average of 0.09 per cent. Values over 0.13 per cent. are to be looked upon as pathologic. Physiologic alimentary hyperglycemia, according to their observations, disappears in from one to two hours. Large doses of sugar do not exert a lasting influence on the sugar content of the blood. In some kidney cases, a slight increase of the blood sugar was found which usually rapidly disappeared during their stay in the hospital. In these cases, abnormal alimentary hyperglycemia did not occur.

<sup>1</sup> Berl. klin. Woch., 1913, No. 19.

<sup>2</sup> Münch. med. Woch., 1913, No. 41.

<sup>3</sup> Ugeskrift for Laeger, October 2, 1913.

Their studies demonstrated that increased blood-pressure and increased blood-sugar are entirely independent of each other. In affections of the stomach, no increase of the sugar was found, while in pancreatic disease, a considerable increase was noted. Nervous disturbances showed no abnormal values. In a case of hyperglycemia, an increased blood-sugar content, in connection with an increase of the reducing substance in the blood-corpuscles, was demonstrated. In diabetes, there usually occurs increase of the blood-sugar, but this hyperglycemia is not in proportion to the glycosuria which can occur without hyperglycemia. The range of values for the seven cases of typical diabetes which were studied was from 0.071 to 0.265 per cent.

Lampe and Strassner<sup>1</sup> have used the Band method with slight modifications for observations on the blood of diabetics on different diets. They found that on certain forms of diet in some cases a disappearance of urinary sugar was accompanied by the sinking of the blood-sugar to normal; while in others, during the periods of freedom from urinary sugar, the hyperglycemia persisted. Variations of the blood-sugar, independent of the diet, are dependent upon severe disturbances of the carbohydrate metabolism.

Purjesz<sup>2</sup> has ascertained that in normal individuals the sugar-content of the blood shows considerable variations within normal limits. He found the greater part of the blood-sugar under normal relations to be contained in the blood-plasma and the lesser part in the blood-corpuscles. In pyrexia, the sugar content of the blood-corpuscles increases during the period of fever. Increased functioning of the thyroid gland showed lessened values, and in Addison's disease the determinable amount of sugar in the blood was slight. In pneumonia, hyperglycemia was usually present in consequences of the pyrexia, even in the unfavorable cases. In miliary tuberculosis and typhoid fever absolute hyperglycemia was demonstrable in the cases studied.

Tachan<sup>3</sup> says there is a pronounced increase in the blood-sugar in every case of true diabetes, and this occurs even before sugar appears in the urine. He emphasizes the importance of estimating the sugar-content of the blood in order to find the true condition in this disease. It serves as an early index of the extent of the disturbance to the metabolism, and as a guide to the progress of the case under treatment. Ingestion of 100 grams of grape sugar does not increase the proportion of the sugar in the blood in healthy persons, but when there is a pathologic disturbance of the metabolism of sugar this proportion is distinctly increased. This fact is of great practical importance, as hitherto we have had to depend upon examination of the urine alone. The author found 0.1 per cent. as the upper limit after the ingestion of 100

<sup>1</sup> Med. Klinik, September 7, 1913.

<sup>2</sup> Wien. klin. Woch., September 4, 1913.

<sup>3</sup> Deutsch. med. Woch., April 10, 1913.

grams of sugar with 50 grams of white bread, fasting, in 30 healthy persons. In diabetics, however, the sugar-content of the blood runs up to 0.2 per cent. or over, even when there is no glycosuria.

Part,<sup>1</sup> from a study of 13 cases of nephritis in which the blood-pressure values and the blood-sugar values were compared, concludes in agreement with Bing and Jacobson<sup>2</sup> that there is no fixed relationship between hypertension and the sugar-content of the blood. His study showed only that hyperglycemia may often occur in those cases which are accompanied by uremia, a fresh apoplexy or eclampsia. To look upon adrenalinemia as a common cause for hyperglycemia and hypertension, as earlier suggested by Neubauer, and more lately by Hagelberg, is, therefore, not permissible.

In a series of 35 chosen cases of other diseases, the author found some with normal, and others with increased, values for the blood-sugar, which speaks against the assumption of a definite common cause for hypertension and glycemia.

Farini<sup>3</sup> has studied 20 patients with high blood-pressure, 10 having kidney disease, and 10 having pronounced arteriosclerosis. Some of the nephritic patients showed a hyperglycemia, while others did not. On the other hand, the hypertension of arteriosclerosis unaccompanied by functional kidney lesions, showed no increase in the blood-sugar. From these studies, the author concluded that in the pathogenesis of arteriosclerosis the hyperfunctioning of the adrenal bodies plays no etiologic, and scarcely an important part.

**Experimental.** Thannhauser and Pfitzer<sup>4</sup> have investigated the effects of intravenous injections of grape-sugar on the sugar-content of the blood and of the urine. The cases investigated consisted of three normal persons, 5 cases of liver affections, 4 cases of kidney affections, 3 cases of mild diabetes, 2 of moderate diabetes, 1 of severe diabetes and 1 of Addison's disease. They found that in all cases the intravenous injection of a 7 per cent. grape-sugar solution in ascending doses, beginning with 5 grams, was accompanied by no notable disturbance, on two occasions only there being a slight rise of temperature. The normal cases, fifteen minutes after the injection of 20 grams of the sugar solution, excreted a fraction of a gram of sugar in the urine. The excretion of the sugar in the urine after large injections did not increase proportionately with the amount injected. The blood-sugar values in normal individuals, fifteen minutes after the injection of 500 c.c. of the 7 per cent. solution, returned to normal. The cases of liver disease for at least an hour after the injection revealed a hyperglycemia without glycosuria. In chronic nephritis there was at first a raised sugar-content in the blood with a very rapid descent to the original values in fifteen minutes,

<sup>1</sup> *Deutsch. med. Woeh.*, January 9, 1913.

<sup>2</sup> *Loc. cit.*

<sup>3</sup> *Gazzetta degli ospedali e delle Cliniche*, August 3, 1913.

<sup>4</sup> *Münch. med. Woeh.*, September 30, 1913.

and, at the same time, a very slight glycosuria. In diabetes mellitus, the severe cases showed an excretion of the entire amount of injected sugar, while the light cases showed an excretion of only a moderate fraction of the injected sugar. The blood-sugar curve in the severe cases was not steep, but long drawn out and flat, and, in the milder cases, the values were similar to the normal.

It has been shown by Ringer that the administration of propionic acid to phlorhizinized dogs is followed by the elimination of "extra glucose," equal in amount to that capable of being formed from the propionic acid if all three carbon atoms are used in the formation of glucose. This led Greenwald<sup>1</sup> to compare this glucose formation to that in appropriate cases of diabetes mellitus. In 3 cases of this disease, on one or two occasions, he administered propionic acid with the result that, on all occasions, with one exception (very slight diabetes), there was an increase in the excretion of glucose. In the first experiment, the "extra glucose" was almost exactly equivalent in amount to the propionic acid ingested. Later, when the G : N ratios were lower, indicating an increased capacity for the oxidization of carbohydrates, the amount of glucose formed from the propionic acid was much diminished.

Ringer, Fränkel, and Jonas<sup>2</sup> have carried out several series of experiments in an investigation of the chemistry of gluconeogenesis. In one series carried out on phlorhizinized dogs, it was found that isobutyric acid and isobutyl alcohol gave rise to glucose probably by undergoing demethylation and by giving rise to normal fatty acids (propionic acid). Isovaleric acid does not give rise to glucose, but to large quantities of aceto-acetic acid, acetone, and betahydroxybutyric acid. Isocaprylic acid was found to give rise to glucose probably having, by a process of demethylation, formed normal valeric acid which becomes oxidized to propionic acid. Isobutyric acid, in certain cases, possesses very marked antiketogenic properties. It is suggested by these experimenters that isovaleric acid is one of the intermediary stages in the catabolism of leucine, and, likewise, that isobutyric acid may be an intermediary body in the catabolism of valine.

In another series of experiments performed on phlorhizinized animals, these authors<sup>3</sup> have found that succinic, malic and perhaps also malonic acids give rise to extra glucose. Evidence is presented to the effect that succinic acid is an intermediary body in the metabolism of glutamic acid, ornithin and prolin, which accounts for the conversion of these substances into glucose. It is suggested that malonic acid may arise in part from the catabolism of aspartic acid, and, likewise, that hyasine in its catabolism, passes through a glutaric acid stage which accounts for its own conversion into glucose.

<sup>1</sup> Journal of Biological Chemistry, 1913, vol. xvi.

<sup>2</sup> Ibid., vol. xiv.

Ibid.

**Metabolism.**—During the four years from 1908 until 1912, Benedict and Joslin<sup>1</sup> have made numerous metabolic observations on diabetic patients by means of the calorimeter and the respiration apparatus. In these studies they considered the rate of the pulse, the body temperature, and the body weight in addition to the chemical conditions. They found that the average rate of the pulse for all diabetics studied was 65 per minute (minimum) and 81 (maximum). For normal persons studied, these figures were 54 and 74. The temperature in all cases, with one exception, was within the normal limits. The loss of weight almost throughout the severe cases varied from 5 to 48 per cent. of the original high weight. The average loss of weight in the authors' patients was 22.7 per cent. In their studies of the total metabolism, they found that the results, as expressed through the bed calorimeter and the respiration apparatus, corresponded very constantly. The average excretion of carbonic acid in the stool calorimeter was 3.54 c.c. per kilo of body weight per minute. With the bed calorimeter these figures were 3.47 c.c., and with the respiration apparatus 3.19. The total average of values obtained with the bed calorimeter and the respiration apparatus was 3.33 c.c. per kilo of body weight per minute, which can be taken as the average carbonic acid production of the resting, nourished patients with severe diabetes who were studied. The consumption of oxygen was 4.85 c.c. per kilogram of body weight per minute with the stool calorimeter. The bed calorimeter showed values of 4.66, and the respiration apparatus 4.41. The average values obtained for the consumption of oxygen with the bed calorimeter and the respiration apparatus was 4.54 c.c. per kilogram of body weight per minute.

In severe diabetes, nearly all respiratory quotients approach the value of 0.74 when the patients, in nourished condition, are lying at rest. Respiratory quotients above 0.74 are to be looked upon as prognostically favorable in severe diabetes because they show a greater supply of carbohydrate in the body.

The average production of heat in all of the experiments was 1.35 calories per kilogram of body weight per hour with the stool calorimeter, and 1.15 calories with the bed calorimeter.

Of the 19 severe cases studied, 18 showed an intensity of the metabolism, as measured by consumption of oxygen, which was higher than that of the normal controls. The single exception among these 19 showed higher values than the controls with which she was compared, but these controls showed a distinctly lowered metabolism, so that the average consumption of oxygen for the four normal controls was less than in this case.

The average consumption of oxygen in all the cases of severe diabetes with the exception of the one mentioned, was 4.54 c.c. per kilogram per minute, while in the normal controls the average was 3.75. This

<sup>1</sup> *Deutsch. Archiv f. klin. Med.*, 1913, exi.

corresponds to an increase of 0.79 c.c. per minute over the normal, or about 20 per cent.

The figures show that the caloric equivalent of carbonic acid generally in mild cases of diabetes is somewhat higher than in severe cases. The average for all cases, if the patients are nourished, is 3.30 calories, while in the experiments where nourishment was omitted it was 3.37 calories.

For every gram of carbonic acid, 3.26 calories were produced in severe diabetics in the nourished state, and 3.31 calories for every gram of oxygen.

These researches prove sufficiently that the metabolism in diabetes is accelerated, and from these results *pari passu* there is a tendency to acceleration of the metabolism in proportion to the intensity of the diabetes. If diabetic patients with acidosis show an accelerated metabolism, why should not an artificially produced acidosis, in normal men, act in the same way? The authors have considered this point. In two normal persons they estimated the consumption of oxygen and production of carbonic acid before and after the subjects had been placed on a diet free from carbohydrates. In both of these experiments, there was a definite acceleration of the total metabolism. This rise in the production of carbonic acid is explained through the change from a carbohydrate to a fat diet.

In a late experiment carried out in the author's laboratory, a man, after fasting thirty-one days, showed no distinctly greater amounts of beta-oxybutyric acid in the urine than the two subjects on a carbohydrate-free diet who were studied.

The metabolism in this man was not accelerated. On the contrary, there was an increasing loss of metabolic activity the longer the fast lasted. It might be possible to attribute the increase of metabolism in diabetes to the intensity of the acidosis, if in acidosis alone we could demonstrate a heightened metabolism. Whether the beta-oxybutyric acid molecule circulating in the blood stimulates cell activity, or whether this effect is brought about by a loss of alkalinity of the blood, we cannot say. Whatever the cause may be, apparently the body can, up to a certain stage, accustom itself to this irritation or stimulation, and through time react less and less to its influence. The fact that 55 grams, or more, of beta-oxybutyric acid can be excreted by diabetics, without a greater acceleration of the metabolism than takes place in normal individuals on a carbohydrate-free nourishment who only excrete 4 to 5 grams of this acid, would seem to support this idea.

Clinical experience with diabetic patients shows that an acidosis of moderate intensity which is called forth suddenly by withdrawal of the carbohydrates is more dangerous than a distinctly severe acidosis which is caused through a gradual withdrawal of carbohydrates. In this manner, on entrance into a hospital, the sudden withdrawal of

carbohydrates can bring on an acute attack of coma. It is often surprising how small an amount of beta-oxybutyric acid there is in the urine of such patients.

Pribram and Lowy<sup>1</sup> carried out extensive metabolic studies on 14 cases of diabetes mellitus with the view of determining the relations between the colloidal nitrogen, the total nitrogen, and the urinary sugar. In reviewing these cases they recognize four groups: (1) Severe cases, with a tendency to coma, in all of which the colloidal nitrogen is greatly increased; the proportion of colloidal nitrogen to total nitrogen moderately increased and the proportion of urinary sugar to colloidal nitrogen is high; (2) severe cases without coma in which the colloidal nitrogen is moderately increased, the proportion of colloidal nitrogen to total nitrogen moderately high, and the proportion of urinary sugar to colloidal nitrogen very high; (3) moderate cases in which the colloidal nitrogen is high, the proportion of colloidal nitrogen to total nitrogen high, and the proportion of urinary sugar to colloidal nitrogen relatively small; (4) mild cases in which the amount of colloidal nitrogen is somewhat raised, the proportion of colloidal nitrogen to total nitrogen moderately high, and the proportion of urinary sugar to colloidal nitrogen slight.

As to prognosis in diabetes, the authors demonstrate that, from their work in cases of no great severity, the amount of colloidal nitrogen increases with the severity of the cases, while in severe cases the colloidal nitrogen, apparently as a result of retention, decreases. An improvement of the mild cases is accompanied by a lessened excretion of colloidal nitrogen, while improvement in severe cases is accompanied by a rise in the colloidal nitrogen. These relations enable us to follow the effects of therapeutic procedures on the disease. An increase in the proportion of urinary sugar to colloidal nitrogen prognosticates an unfavorable conclusion.

From several series of experiments carried out on healthy dogs, phlorhizinized dogs and a human patient with bronze diabetes, Woodward<sup>2</sup> has found that the muscles of glycogen-free animals form some sarcolactic acid (about 30 per cent. of the normal). This acid cannot come from glycogen, but must arise from preformed sugar or directly from certain amino- or fatty-acids. The muscle of a case of severe human diabetes was found to form even less lactic acid than that of fully phlorhizinized dogs. This fact suggests an impaired power to dissociate glucose on the part of the diabetic muscles, since such muscles are bathed with an abnormal quantity of sugar which, if available, should yield more lactic acid than is found in the muscle of phlorhizin diabetes. With dextrose, nitrogen ratios of approximately 3.65 to 1 postmortem analyses of dog muscles and livers show no glycogen.

<sup>1</sup> Zeit. klinische Med., 1913, lxxvii.

<sup>2</sup> Journal of Biological Chemistry, 1913, vol. xiv.

With ratios of 2.8 or 3.0 to 1 this is not necessarily the case, and we cannot assume that with a constant dextrose to nitrogen ratio of 2.8 to 1 an animal is free of glycogen.

**Association.**—The association of *diabetes* and *tuberculosis* was discussed in these pages last year. Frew and Garrod<sup>1</sup> have studied 49 cases of tuberculous meningitis in which the diagnosis was confirmed by autopsy, except in three cases, and in these the tubercle bacillus was found in the cerebrospinal fluid. In 15 of the 41 cases (36.6 per cent.), glucose was found in the urine at some period in such quantity that when equal volumes of urine and Fehling's solution were mixed when hot, but without reboiling, conspicuous reduction occurred. In the earlier cases examined, an osazone, with the appearance and melting-point of glucosazone, was obtained, the urine was found to be dextrorotary, and estimations of the glucose yielded figures between 0.25 and 1 per cent. In 11 of the remaining 26 cases, partial reduction of the hot Fehling's solution was obtained without reboiling, and this at the same period of the disease at which pronounced glycosuria appeared in the other 15 cases. In the remaining 15 cases of the series, no reduction of Fehling's solution was obtained at any time. In each case, daily, or more frequently, examinations were made, from the time the diagnosis of tuberculous meningitis was made until the death of the patient. Once developed, the glycosuria persisted for the remaining days of the patients' lives, and, in the great majority of instances, the sugar only appeared in the two last days of life.

In their clinical features, the glycosuria cases presented no striking differences from those in which no sugar appeared in the urine, nor was there any obvious influence of sex or age in this respect. As far as could be judged, the liability to glycosuria is no greater at one age than at another. Certain clinical features, such as the duration of the illness, the degree of fever and depth of unconsciousness, appeared to be equally without influence on the development of glycosuria. The organs which play recognized parts in the causation of glycosuria were examined with special care. In no instance did naked eye or microscopic examination of the pancreas show any morbid changes in that gland to which the occurrence of the glycosuria could be ascribed. The same may be said of the thyroid and adrenal glands. In some cases miliary tubercles were present in them, but this was equally true of cases in which no sugar was excreted and of the glycosuric cases. The characters and distribution of the tuberculous lesions elsewhere than in the meninges differed in different cases, but, as far as could be judged, the differences of distribution bore no obvious relationship to the presence or absence of glycosuria. In a number of fatal cases of tuberculosis without meningitis, in which the urine was examined during the last days of life, no sugar was ever found. It seems highly

<sup>1</sup> Lancet, January 4, 1913.

probable to the authors that the presence of the meningitis is the factor which determines the occurrence of glycosuria.

**Diabetic Coma.** Ehrmann<sup>1</sup> has made extensive experimental studies of coma. He was able to produce this state in rabbits through the administration of the sodium salts of the butyric acids (butyric acid, 1 beta-oxybutyric, aceto-acetic acid—beta-ketobutyric acid). These acids all act as poisons to the central nervous system, especially the cerebrum, the respiratory centre and the vasomotor centre. If the action on the vascular system is predominant, the cardiovascular form of coma is induced. These experimental forms of coma resemble very closely the form seen in human diabetes. The favorable action of sodium bicarbonate in this condition is not due to a neutralization of the acid by the alkali, but rather to the fact that the alkali stimulates the excretion of the poisonous butyric acid, and, in addition to this, acts as a stimulant to the vasomotor system. It does not cure coma, but it is useful in aborting it when given early. The ferric chloride urine test may be negative, even in incipient coma, but, after the administration of alkali, this test becomes positive. The patient is in greater danger, the less the response to this test. The observations of Ehrmann explain the origin of diabetic coma and emphasize the importance of recognizing the action of the toxic fatty acids on the centres of respiration, as expressed through the peculiarly low, deep type of breathing. The early recognition of this toxic action on the respiratory centres should enable us to institute treatment in time to ward off the attack of coma. The toxic action on the respiratory centres spreads to other portions of the central nervous system until coma results. That the brain is predominantly affected in this condition the author considers is shown by the fact that the needed doses of sodium bicarbonate administered are not in proportion to the body weight, but in proportion to the weight of the brain. The small amount of acetone found in the urine of animals with coma excludes this body as a cause of the condition. When the action of these poisonous acids is predominantly on the cardiovascular system, sudden death may ensue. This injury to the vascular system is accompanied by low blood-pressure, and the author emphasizes the importance of ascertaining the blood-pressure in cases when impending coma may be suspected. In his experiments, the intravenous injection of sodium bicarbonate in cases of coma raises the blood-pressure; hence, this drug evidently has a stimulating action on the vascular system.

Rolly's<sup>2</sup> researches on the electric tension of the blood, including that of a number of cases of diabetic coma, show that, in some cases of coma, the blood may be moderately alkaline, while in others it may be slightly acid. In one patient who died, the reaction was normal.

<sup>1</sup> Berl. klin. Woch., January 13, 1913.

<sup>2</sup> Medical Clinic, April 13, 1913.

These findings convinced Rolly that fatal termination in this condition cannot be entirely due to the action of acids as such. Patients with an acid reaction who had been given enough sodium bicarbonate to render the reaction normal did not show general improvement, and the fatal outcome was not averted. Diabetic coma is, therefore, not a pure acid intoxication or acidosis in the sense of Naunyn.

In Blum's<sup>1</sup> study of the condition in which he discusses three types—the cardiovascular, the dyspneic, and a combination of the two—he found that the blood-pressure is not always subnormal at first, as stated by Ehrmann.<sup>2</sup> Concerning the ocular tension, he says that the loss of water alone cannot explain this reduction; the salts must also be involved. Large doses of alkali are liable to return the tension to normal.

**Treatment.** Lepine,<sup>3</sup> in a review of the progress in the treatment of diabetes during the last fifty years, lays stress on the pathogenesis of the disease which he considers to be due to a decreased glycolytic function. Progress in the dietetic treatment of the condition has been mainly in recognizing the importance of oatmeal and similar cures. He explains the action of these through a transformation of the intestinal flœæ. With this transformation, the bacteria oxidize a portion of the sugar formed in the intestines, and, in this manner, supply to the organism ternary products and thus reduce the amount of sugar absorbed in the intestines. Drugs are useful when applied to certain conditions in the disease, but, on the whole, they exert little influence upon the disease itself. Sodium bicarbonate is an exception, for this drug is indispensable in acidosis. In its administration, Lepine uses an isotonic solution and preferably gives it by intravenous injection. It should be given before the coma develops in order to be effectual; afterward, it affords only more or less transient relief.

Little, if anything, has been suggested during the year in the *dietetic treatment* of diabetes. The same general principles govern our direction of the diet—the tolerance for carbohydrate and the threat of acidosis.

Tausz<sup>4</sup> emphasizes the importance of determining the tolerance for albumen as well as for carbohydrates, and, in the renal form of the disease, the tolerance for sodium chloride should be ascertained, and the diet so arranged as to help the nephritic condition as well as the diabetic. He looks upon the benefit derived from the oatmeal and vegetable days as being due to their content of alkali, which tends to neutralize the acidosis. The kat-ions in this diet have a high catalytic power on the special ferment. He believes that it may yet be possible to increase the production of ferment in some manner, or, at least, to mobilize them.

This possibility has been suggested by recent experimental work in which cane-sugar was added to dog serum and remained unmodified.

<sup>1</sup> Berl. klin. Woch., November 7, 1913.

<sup>2</sup> Loc. cit.

<sup>3</sup> Ibid., March 17, 1913.

<sup>4</sup> Med. Klinik, June 8, 1913.

But, after the dog had been given an intravenous injection of 10 c.c. of a 5 per cent. solution of glucose, and cane-sugar then added to the drawn serum, the sugar was promptly split, which suggests that the body produces protective ferments against carbohydrates, and may be led to do so at will.

Lauritzen<sup>1</sup> calls attention to the importance of limiting the intake of albumen in diabetes. He believes the progressive tendency of the condition is best counteracted by this means. In mild cases, he allows only 2 grams of albumen per kilo of body weight, and interposes periods when only 1.5 grams are allowed. In very severe cases, he permits no more than 1 gram of albumen per kilo of body weight, and interposes periods when only 0.5 grams are given.

The favorable action of the lactic acid bacillus on diabetes forms the subject of several reports in the literature. In discussing this mode of treatment, Horowitz<sup>2</sup> remarks that in cases in which there is no indican in the urine and no auto-intoxication, definite causative factors usually produce the glycosuria, as thyroidectomy, ether narcosis, which probably causes a parenchymatous degeneration of the liver, etc. In the majority of cases, however, the indican output is in close relation to the sugar output. In a series of tests made by the author on starch digestion by pancreatic juice, both human and canine, carried out for a period of several weeks, he found that the digestion of the starch is accomplished much more slowly in the presence of the bacillus bulgaricus than when pancreatic juice is used alone. The bacillus generates free lactic acid, and, in order to determine whether the interference with the digestion of starch was accomplished by the bacillus alone or by its generated acid, a solution of the acid of similar strength to that present in the culture, was used, and the result on the starch digestion obtained was the same. This shows that the bacillus bulgaricus generates free lactic acid, and the presence of this acid interferes with the rapidity of starch digestion. While it is agreed that, in cases that have come to autopsy, there are changes in the pancreas, especially in the islands of Langerhans, and that these changes are probably present in all cases of diabetes, with perhaps irritation and changes in the adrenals, thyroid, nervous system and hypophysis, still these changes are also caused by auto-intoxication.

By correcting and curing the auto-intoxication, Horowitz says, one can remove the irritating influences on the sugar-regulating apparatus. Bacillus bulgaricus destroys putrefaction, and so overcomes the auto-intoxication: the bacillus changes the reaction of the intestinal tract from an alkaline to an acid condition; carbohydrate digestion is inhibited or is rather very much slower in the presence of this lactic acid; by thus lengthening the time of carbohydrate digestion, only small amounts

<sup>1</sup> Therapie der Gegenwart, February, 1913.

<sup>2</sup> Medical Record, January 25, 1913.

of sugar are formed and absorbed; permitting only small amounts to be formed and absorbed increases gradually the tolerance for carbohydrates until a normal tolerance is established.

Beveridge<sup>1</sup> discusses the effect of the administration of the Bulgarian bacillus in diabetes, reporting the results in 176 cases, and giving in more or less detail a description of 11 cases. He divides the cases into two classes: (1) glycosuria without acidosis; (2) glycosuria with acidosis.

In cases of the first class, the symptoms entirely subsided during treatment. Only seven still have traces of sugar, and, if they are kept under observation from time to time, he believes they will remain in a fairly normal state. In cases of the second class, the results have not been so marked, although all the patients have shown considerable improvement, with most of the major symptoms disappearing. The gain in weight has averaged from three to eighteen and a half pounds, and in many the polyuria has diminished from eight quarts a day to three quarts and one pint. The proportion of recoveries, however, is very small, and out of 79 cases of acidosis he says that 5 have recovered and 27 have apparently been greatly benefited; the rest, with the exception of 2, remaining about the same as when first observed. These 2 patients, both under fifteen years of age, have since passed away.

Beveridge concludes that the efficacy of this culture in diabetes is undoubtedly due to its power to prevent intestinal putrefaction; that the stimulating effect upon the pancreas by its acidity is potent; that its power to convert starch into lactic acid is an important factor; that by relieving auto-intoxication many of the symptoms in diabetes are stopped; that the use of the  $\alpha$ -ray in diagnosis is most valuable.

The necessary analysis of the gastric contents should be made so a consistent method may be followed in treatment.

The routine examination of the blood, not only for acetone, but sugar, is advisable.

The prevention of this disease and the overcoming of its progress are unquestionably possible, and he believes that by systematic, thorough care of all glycosurias in the first class, a permanent recovery will be the reward.

Glycosurias of the second class do not apparently respond, although the patient's condition seems to be greatly benefited.

The use of this culture in diabetes is far superior to that of opium, and offers the only rational internal therapy really of value.

Blodgett<sup>2</sup> reports unfavorable results in using this method of treatment with 5 cases.

Arnheim was the first to prove that rectal injections of grape-sugar were of greater value than equivalent amounts administered by the mouth. Luthje<sup>3</sup> has demonstrated that a greater part of the grape-

<sup>1</sup> New York Medical Journal, July 12 and 19, 1913.

<sup>2</sup> Medical Record, June 14, 1913.

<sup>3</sup> Therapie der Gegenwart, May, 1913.

sugar administered per rectum disappears without an increase of the glycosuria. He has used this method of administration in 10 diabetics, giving a drop at a time by the proctoclysis method. Most patients can absorb very well, 1 to 2 liters in the course of a day. In a 5.4 per cent. solution this would be equivalent to from 50 to 100 grams of sugar. He has repeatedly witnessed the subsidence of acidosis under the influence of this treatment. The proportion of sugar in the blood increases under this sugar solution proctoclysis, while it remained unmodified in 3 persons who were given salt solution by the same technique instead of the sugar. Other patients who sipped the sugar solution, taking as long to ingest a liter as when it was given by proctoclysis, did not show an increase in the sugar content of the blood in the same way as when it was given per rectum. This proves that it was absorbed and assimilated better from the rectum than from the alimentary tract.

In the treatment of cardiovascular symptoms in diabetic coma and the stage preceding, Ehrmann<sup>1</sup> states that long before coma develops we can detect the poisonous action of the butyric acids by carefully watching the cardiovascular system. If it shows signs of weakness, we can ward off coma by supporting it with the proper drugs. These drugs must be pushed to support the cardiovascular system just as sodium bicarbonate is pushed until the urine is alkaline or the ferric chloride test shows the most intensive response. He cites 11 cases in which he was enabled to avert impending coma by supporting the cardiovascular system by subcutaneous injections of camphor, caffeine, or some digitalis preparation by the mouth. One patient he has succeeded in keeping in this stage of pre-coma for two years. This man, aged forty-two years, frequently had what Ehrmann calls "the pre-coma expression," which resembles the sleepy phase following epileptic seizure. The blood-pressure varied from 140 to 150. After a few months, a slight attack of coma developed, when the respirations became slow and deep, the eyeballs were soft, and the blood-pressure was only 100 mm. The subcutaneous injection of camphor tided the patient over the danger-point and he returned to comparative health, although he still at times has periods of deep costal breathing.

### THE DUCTLESS GLANDS.

This year it has been thought proper to review our present knowledge of the physiology and interrelationships of all of the ductless glands instead of going into a detailed account of the advance in our knowledge of certain of these structures. In addition to a brief review of the year's literature, the writer has made use of the excellent works of Biedl, Swale Vincent, and Noel Paton.

<sup>1</sup> Berl. klin. Woch., August 4, 1913.

**The Thyroid Gland.** The chemical structure of the thyroid secretion is characterized by a comparatively large content of iodin which occurs in organic combination. This organic combination probably acts upon the organism in a different manner from inorganic iodine. It exists to the extent of 0.3 to 0.9 mg. per gram of the dry gland substance.

Jones and Tatum<sup>1</sup> have found that, in rabbits, this iodin content is increased directly by feeding the animals with commercial desiccated thyroids, and indirectly by intravenous injections of serum from hyperthyroid rabbits. It is decreased by intravenous injections of the serum of thyroidectomized rabbits. Following injections of normal serum, the iodin content was increased, decreased or constant, according to individual variations in thyroid activity.

Iodin is absent in the thyroid of newly born children.

Fenger<sup>2</sup> has shown that fetal thyroid tissue possesses a strong selective affinity for iodin; that the glands of beef fetuses contain an appreciable amount of iodin as early as the third month of intra-uterine life, and that the iodin content increases proportionately with the age of the fetus. He also demonstrated that the presence of this active principle in a gland is an indication of its relative physiological activity long before the maturity of the fetus. From a study of 705 beef fetuses, he found that the normal female fetal thyroids show a higher content of iodin, and seem, therefore, to possess greater functional activity than the male fetal glands. Fetuses possessing enlarged thyroids on the whole were considerably smaller than average fetuses of the same age with normal thyroids.

The herbivora show a higher iodin content of the gland than the carnivora.

Seidell and Fenger<sup>3</sup> have noted a marked seasonal variation in the percentage of iodin present in the normal-sized thyroid of the sheep, beef, and hog. There is, in general, about three times as much iodin present in the glands in the months from June to November as in the months between December and May. A seasonal variation of the size of the gland was observed in sheep, and beef, but not in the hog. The glands were found to be larger during the months in which the lower iodin content was observed. This fact would seem of importance in obtaining a standardized commercial product of the gland.

The iodin exists as a protein combination—iodothyreoglobulin.

Koch<sup>4</sup> found that the full activity of the thyroid tissue is contained in the thyreoglobulin fraction. The full iodin activity per iodin unit is still present in the metaprotein fraction from this globulin, although the iodin content in the metaprotein fraction has been increased over threefold that of the globulin itself. The other products of the hydrolysis

<sup>1</sup> Archives of Internal Medicine, August, 1913.

<sup>2</sup> Journal of Biological Chemistry, May, 1913.

<sup>3</sup> Ibid., January, 1913.

<sup>4</sup> Ibid., March, 1913.

studied, primary albumose, iodothyroin, and secondary albumose show a gradual decrease in activity per unit of iodin in the order given. The amino-acid fractions still contain very small amounts of iodin and are either extremely low in activity per unit of iodin or entirely inactive. Tetra-iodo-histidin and anhydrid and iodotryptophan possess no thyroid activity, as determined by the Hunt method.

The results of the removal of the thyroid gland in young rabbits are a checking of the cartilaginous ossification, with a consequent decrease in the length of the bones. Degenerative changes take place in the epiphyseal line; there is an enlargement of the hypophysis cerebri; the ovaries degenerate, and some follicles ripen precociously; and the testes show decreased development. Analogous changes occur in other animals.

Tatum<sup>1</sup> in a morphological study of experimental cretinism has found that degenerative changes occur in practically every parenchymatous organ. In regard to the changes in the glands of internal secretion, his findings corroborate the statements of Cushing in regard to hypophysectomy, that removal of one gland of internal secretion results in changes in all the other glands. In Tatum's studies carried out on litters of young rabbits, degenerative changes predominate in the hypophysis, thymus, ovary and testis, while hyperplasia is seen in the islands of Langerhans and the medullary portions of the adrenal glands.

In the child, decreased growth occurs at the epiphyseal line. There is shortening of the base of the skull and prominence of the cranium. The sexual glands remain undeveloped, and the secondary sex organs are infantile in character. There is pituitary enlargement, and marked mental deficiency. In the adult, removal of the gland results in the condition of cachexia thyreo-priva. This is characterized by muscular weakness and mental apathy, thickening of the skin, which becomes white and wax-like, and a peculiar sogginess of the subcutaneous and submucous tissues. These changes give rise to an appearance of fatness. The skin is cold and dry, and degenerative changes in the hair occur. Disturbance of the sexual function is also brought about.

The clinical study of hypothyroid states bears out the evidence obtained through experimental removal of the gland. Underfunctioning of the thyroid may be congenital, infantile, developing in the early years of life, or may occur in later life. Cretinism and myxedema may vary in degree, according to the extent of disturbance of function.

The effect of the thyroid secretion on metabolism shows that the removal of the gland decreases the metabolism of proteins. This is also said to be true of the metabolism of fat.

In regard to its relation to carbohydrate metabolism, it has been shown that after removal of the gland large amounts of sugar may be

<sup>1</sup> Jour. of Experimental Medicine, June, 1913.

administered without the appearance of glycosuria, especially if the parathyroid glands are left intact. This antimobilizing effect on sugar through removal of the thyroid may be brought about by its inhibiting effect on the adrenals which normally stimulate mobilization; or, it may be due simply to a lessened check on the antimobilizing function of the pancreas. It would thus seem that the thyroid and adrenals act as stimulators in the mobilization of sugar, and that both of these glands are opposed to the function of the pancreas which inhibits mobilization.

Edmunds,<sup>1</sup> in experiments upon dogs, concludes that the thyroid gland hinders the assimilation of sugar, while the parathyroid glands favor it. The balance between these glands regulates the carbohydrate metabolism.

The effects of thyroideectomy and hypothyroidism may be offset by *transplantation* of portions of the gland into the affected organism.

Katzenberg<sup>2</sup> reports the cases of two children with congenital myxedema who showed no improvement under thyroid treatment, but who displayed marked benefit following grafting of a portion of the mother's thyroid.

The effects of removal of the thyroid and the hypothyroid state are likewise offset by the administration of thyroid substance and extracts of the gland. Brush and Cornell<sup>3</sup> report a case of myxedema coming on in later life which was cured by the administration of desiccated thyroid, and this cure has persisted seven years after the institution of treatment.

Zuber<sup>4</sup> reports the case of a young man who took thyroid treatment for thirteen years. At the age of eight, he was the size of a child of two. Although he developed both physically and mentally under the influence of the thyroid treatment instituted at the age of eight, he never regained the six years he lost, his size and mental condition now being those of a normal youth of fifteen.

The long continued administration of thyroid products brings about a condition of hyperthyroidism in man and the lower animals.

Farrant<sup>5</sup> has carried out an elaborate series of experiments on cats, rabbits, guinea-pigs, and dormice. In these experiments, the animals were fed on thyroid substance in various ways. The cats proved the most resistant to the effects of this substance. The other three sets of animals were very susceptible. The rabbits lived longer than the guinea-pigs. The cardinal symptoms in all were fur changes, loss of weight, weakness, increased appetite, and diarrhea. Tachycardia was

<sup>1</sup> Journal of Pathology and Bacteriology, July, 1913.

<sup>2</sup> Med. Klinik, March 23, 1913.

<sup>3</sup> Archives of Internal Medicine, May, 1913.

<sup>4</sup> Bulletin de la Société de pédiatrie, February, 1913.

<sup>5</sup> British Medical Journal, November 22, 1913.

well marked in the cats and rabbits, but no reliable observations of this symptom could be made in the smaller animals.

The action of thyroid substance and extracts on the circulation has led some authors to the conclusion that the excitability of the vagus on the heart is increased, and that these preparations also increase the excitability of the depressor nerve.

Blackford and Sanford<sup>1</sup> are convinced from experiments that fresh extracts made from exophthalmic glands contain a powerful depressor substance, and that a powerful depressor substance likewise exists in the serums obtained from exophthalmic goitre. The latter substance is present in direct proportion to the clinical acuteness and severity of the disease. The serums from patients with non-hyperplastic thyroids do not have a depressor action. After an active depressor dose of the serum from a case of exophthalmic goitre, the depressor action of the extract of an exophthalmic goitre is weakened or abolished, and the converse of this is also true.

The condition of hyperthyroidism, including Graves' disease, has been discussed from the clinical, pathological, and etiological standpoints rather fully in these pages.

Hypertrophy of the thymus occurs frequently in the hyperthyroid state; but this state is very apt to occur in individuals of the thymic-lymphatic type. Capelle and Bayer<sup>2</sup> conclude that the possibilities of metabolic findings in a number of typical cases confirm the assumption that the thymus and thyroid may both be incriminated in Basedow's disease, and that the symptoms vary as one or the other predominates in the production of symptoms. The data seemed to show that the predominance of symptoms for which the sympathetic system is responsible points to the thyroid as chiefly to blame; while the predominance of vagus symptoms points to the thymus.

In cases with much exophthalmos, much excited heart action, with tendency to fluctuation of temperature and trophic disturbance, the trouble can be referred to the thyroid. In cases with only slight exophthalmos, with pronounced subjective heart disturbances but no corresponding alteration of the pulse, with sweats, diarrhea and dyspepsia dominating the clinical picture, the blood modified according to the Kocher formula, with an area of dulness over the thymus region and a tendency to myasthenia, the thymus is involved.

Schumacher and Roth<sup>3</sup> report the case of a young woman who had primary, and very severe, exophthalmic goitre, with enlarged thymus and extreme myasthenia. After the employment of ordinary measures for ten weeks no benefit was apparent, but, upon removal of the thymus, the muscle weakness rapidly improved. A few months later all the

<sup>1</sup> American Journal Medical Sciences, December, 1913.

<sup>2</sup> Beiträge zur klin. Chir., September, 1913.

<sup>3</sup> Metteil. aus den Grenzgeb. der Med. und Chir., 1913; No. 4.

symptoms again appeared, and a partial thyroidectomy was performed. The authors say that the recovery after this operation was so rapid that the general condition must have been persistently good, and it seems plausible to assume that the removal of the thymus improved conditions and prepared the way for the later successful thyroidectomy.

Many authors attribute an antitoxic function to the thyroid. Administration of the gland or its extracts has been said to raise the opsonic index in both man and other animals, while extirpation of the gland brings about a reduction of the phagocytic power of the leukocytes and of the opsonic index.

Thyroidectomized dogs are said to have shown a marked diminution in the hemolytic, as well as the bacterial, complement.

Farrant<sup>1</sup> obtained the thyroids from fifteen horses that had received increasing doses of diphtheria toxin for a period varying from a year to eighteen months. It was found that they presented a varying degree of hyperplasia, but that when they were arranged in order from the highest degree of hyperplasia to the lowest they were in the reverse order of the antitoxic value of the serum. The apparently normal thyroid corresponded to the serum with the highest antitoxic value. A number of experiments were carried out on guinea-pigs and rabbits with diphtheria toxin, in addition to the observations made on the equine thyroids. From these experiments, the author concludes that the serum of thyroid-fed animals has practically no antitoxic value.

**The Parathyroids.** The parathyroid glands, four in number, are distributed in two pairs with respect to the median line, an external pair or parathyroids III and an internal pair or parathyroids IV (number of gill cleft from which gland springs). In the carnivora these glands as a rule lie in close approximation to, or even embedded in, the thyroid tissue. While in the herbivora, as a rule, the parathyroids III are situated at some distance from the thyroid. Supernumerary parathyroids may lie in different positions in the neck, and parathyroid tissue has been described as being embedded in the thymus of the rabbit and also that of the cat.

The removal of these glands results in a condition of tetany, which begins with fibrillar contractions of the muscles and gradually grows more severe, with the incidence of tonic and clonic spasms, rapid wasting, and death within ten days. Partial removal of the parathyroid tissues results in a more or less pronounced tendency to tetany, depending upon the amount of the tissue removed. A partial removal may lead to a state of latent tetany which requires some added disturbance in the metabolism to call forth the condition. Werelius<sup>2</sup> has found that thyroparathyroidectomized pregnant dogs (in later stages) seemingly go into convulsions sooner and die sooner than non-pregnant dogs.

<sup>1</sup> Lancet, December 27, 1913.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, February, 1913.

In these thyroparathyroidectomized pregnant dogs, the fetal parathyroids probably do not compensate for the loss of the mother's glands. This leads to the thought that some glands of internal secretion do not functionate in intra-uterine life. The author finds that undoubtedly the earlier in pregnancy thyroparathyroidectomy is performed, the longer will be the postoperative life. The results of this work may in a sense support the parathyroid theory of eclampsia.

It has been found that the primary motor neurons are the structures which are probably involved in this condition of tetany.

Some animals do not develop the condition after what is apparently a complete removal of the parathyroid as well as the thyroid tissues. This may be explained by the fact that the animal may still possess parathyroid tissue, as in the case of the rabbit and also the cat, where such tissue has been found buried in the substance of the thymus gland.

As to the metabolism in this condition, some authors have found a decrease of the calcium content of the blood and brain, as well as an increased output of calcium; while other authors, constituting the majority, have found neither increase in the excretion of calcium nor decrease in the calcium content of the tissues. The relief of tetany through the administration of calcium is probably due merely to a sedative action, and it has been noted that magnesium and strontium will act in the same manner.

Greenwald<sup>1</sup> has discovered a marked retention of phosphorus in parathyroidectomized dogs, and this retention he holds is not due to a preceding retention of sodium or potassium, but is itself primary, occurring either before retention of these alkalies appears, or at the same time.

The total phosphorus of the blood and serum is increased. This may be observed at a time when the tremor is very slight. The increase may amount to as much as 160 mg. per kilo of blood. Greenwald has found that the greater part of this increase is in the fraction which is insoluble in the usual lipoid solvents, but soluble in a mixture of dilute hydrochloric, or acetic and picric acids.

A number of investigators have noted an increase in the protein metabolism after removal of the parathyroid glands. Koeh<sup>2</sup> has shown, experimentally, that digested proteins taken into the body have very toxic effects after parathyroidectomy. These effects are due to products of intestinal, and perhaps, also, products of parenteral, digestion. Such products of digestion are normally placed in some cell molecule, or stored up in some form. In the case of parathyroidectomized dogs, these products are free and act as toxins. According to the author, the parathyroid secretion appears to be concerned with anabolic processes closely related to the building of nucleins.

<sup>1</sup> Journal of Biological Chemistry, May, 1913.

<sup>2</sup> Ibid., July, 1913.

The parathyroid glands seem to influence the carbohydrate metabolism. Partial removal of these bodies lowers the tolerance for sugar. This fact shows an antagonism to the action of the thyroid and the chromaffin system, and may be allied to the antimobilizing function of the pancreas.

Transplantation of the glands has proved to be a difficult procedure, but it has been accomplished, and there are recorded cases where this measure has alleviated the symptoms of tetany.

The administration of gland emulsions, and of the isolated nucleoprotein of the gland, has been successful in suppressing the symptoms of tetany.

**The Thymus.** The thymus usually reaches its maximum growth in proportion to the body weight about the time of birth. After this the growth is slow, and its proportion to the body weight grows less. At puberty, involution of the gland takes place and it decreases greatly in size. These anatomical facts point to the probability that perhaps the chief function of the thymus is exerted during the period of rapid growth and development of the organism, and in all likelihood that it exerts an influence during intra-uterine life.

Removal of the thymus leads to a very distinct train of symptoms in the young. In puppies, after a latent period, muscular weakness sets in with slowness of movements. The bones show a tendency to become softer and break. There are changes in the epiphyses which show marked thickening. The diaphyses in the cortical portion are thicker. Degenerative changes in the muscles also take place. There has been found some evidence of hypertrophy in the cortex of the adrenals, in the thyroid, in the follicles of the spleen, and in the pancreas.

Klose<sup>1</sup> says that the thymus has been proved to be indispensable to growing dogs and that its absence cannot be compensated. Puppies after thymectomy grow abnormally fat and stupid, showing changes in the bones similar to those of rickets and disturbances in the development of the jaws and teeth. A few of the dogs studied developed convulsive conditions resembling tetany. The removal of this gland causes a gradual decrease in the number of leukocytes and administration of extract of the gland leads to an increase. Thymectomy has a marked effect on the blood-pressure, which decreases with increased rapidity of the pulse and finally cardiac collapse. The thymus and thyroid, although closely parallel in their action, cannot compensate for each other. Removal of the thymus leads to hypertrophy of the chromaffin cells and to an excess of adrenalin in the blood. This gland is antagonistic to the sexual glands, and its involution at puberty is probably caused by the development of the gonads.

Transplants of thymus tissue into the abdominal cavity have been successful. Injection of extracts of the thymus is followed by a fall

<sup>1</sup> Jahrbuch f. Kinderheilkunde, December, 1913.

in the blood-pressure. Yokoyama<sup>1</sup> has been able to eliminate or lessen the action of adrenalin on the blood-pressure through injections of extract of thymus, showing that the action of the extract is hypotonic.

Adler<sup>2</sup> has found a constant increase of adrenalin in the blood following treatment with thymus extract. He assumes from this that the adrenal system is striving to weaken or do away with the hypotonic influence of the thymus by an increased adrenalin production.

Some recent experiments have been carried out upon tadpoles by feeding them thyroid and thymus tissue. Those fed on the thyroid tissue show arrest of growth and acceleration of development, while those fed upon thymus show the opposite effect, acceleration of growth and arrest of development.

In castrated cattle, the thymus has been found to be double the size of that in uncastrated cattle. This holds true also for guinea-pigs, and in thymectomized guinea-pigs before sexual maturity the growth of the testes is more rapid than normal. This phenomenon has also been found in dogs. It may represent a reciprocal inhibitory reaction of these glands, or, if considered from the stand-point of influence on growth and development, it may be compensatory in nature. This question was tested by removing both thymus and testes in young guinea-pigs, with the result that after removal of both glands there was marked delay in growth, while removal of one or the other brought about no delay in growth.

Heimann<sup>3</sup> has noted that the secretions of the thymus and ovaries act in an antagonistic manner on the blood-picture with respect to the number of lymphocytes.

The status lymphaticus is a recognized condition in which there is an excessive growth of the lymphatic tissues and of the cortex of the thymus, together with other anomalies of growth and metabolism. The subcutaneous fat is usually excessive, the reproductive organs are infantile in type, and there is a lack of growth of the hair. These individuals have a low vitality, and are more or less liable to sudden death. To attribute this sudden death to overactivity of the thymus seems unwarranted. Hart<sup>4</sup> finds that the thymus may persist and become enlarged but that its functioning may be subnormal. The so-called status thymicolumphaticus is not due to excessive thymus functioning but to a constitutional abnormality expressing itself in disturbances of the whole internal secretory system. The thymus hypertrophy is only one of its manifestations.

Bierring,<sup>5</sup> Goodrich and Theisen have studied four cases which

<sup>1</sup> Virchows Archiv, 1913, vol. cexiv, No. 1.

<sup>2</sup> Ibid., 1913, vol. cexiv, No. 1.

<sup>3</sup> Münch. med. Woch., December 23, 1913.

<sup>4</sup> Virchows Archiv, 1913, vol. cexiv.

<sup>5</sup> American Journal of Diseases of Children, August, 1913.

presented the typical symptom-complex of the status thymicolymphaticus. They find it difficult to conceive that the enlargement of the thymus could be the main causative factor in the deaths of these children.

The hypophysis cerebri, or pituitary body, consists of three parts: (1) A pars anterior, or glandular portion, which develops from an epithelial outgrowth of the anterior part of the alimentary canal. This is the true pituitary. (2) A pars posterior, or pars nervosa, which arises through a down growth from the forebrain in the floor of the third ventricle, and consists chiefly of neuroglia cells. This is the true hypophysis. (3) A pars intermedia, a portion of the true pituitary which is separated from the anterior lobe by a cleft, and is applied closely to the anterior and inferior aspects of the true hypophysis into which some of its cells penetrate.

**Hypophysis (Pars Nervosa).** This portion of the pituitary body is not essential to life, its removal not being followed by fatal consequences. Schimplert<sup>1</sup> has found that the essential principle excreted by the hypophysis can be demonstrated in the embryos of cattle as early as the tenth week.

Lewis and Miller<sup>2</sup> have carried out a number of experiments by feeding both the anterior and posterior lobes to animals, and this feeding of either portion has led to no effect upon the growth. The intravenous injection of extracts of the hypophysis leads to a marked rise in the blood-pressure, which is due mainly to a constriction of the arterioles.

Musser<sup>3</sup> concludes, from his experiments, that prolonged administration of extracts of the entire pituitary body exert a distinct pressor effect on the peripheral vascular apparatus, which persists for an appreciable time after discontinuation of the drug.

The active principle secreted by the hypophysis has not been isolated. In its nature it differs from adrenalin, as shown by both its chemical and physiological reactions. Among other points of difference, it acts as a dilator of the renal arteries and as a constrictor of the coronary arteries. The extract in which this active principle is contained has unfortunately been called pituitrin, which would lead one naturally to think that it is obtained from the true pituitary.

If, after a primary dose of the extract followed by constriction of the arterioles, there be given within an hour a second dose, no constriction of the vessels occurs, and it has been found even that a dilatation, with a fall of the blood-pressure, may follow. The action of this substance on the heart results in an increase in the force of contractions regardless of the vagus. It dilates the pupil of the enucleated eye of the frog, and acts as a stimulant to the bladder in both the dog and cat. On the uterus, it proves to be a powerful stimulant to full contractions,

<sup>1</sup> Monatsschr. f. Geburtsh. und Gynäk., July, 1913.

<sup>2</sup> Archives of Internal Medicine, August, 1913.

<sup>3</sup> American Journal of Medical Sciences, August, 1913.

and it is said to increase the extent of contractions in the intestine. It has a marked diuretic action. This occurs as well after a second dose, when no rise of blood-pressure is noted.

Hoskins and Means,<sup>1</sup> from experiments, have noted that pituitrin, in suitable doses causes diuresis in the anesthetized dog. There is no constant relationship between this diuresis and either systolic pressure or pulse pressure or the ratio between them, although pituitrin diuresis usually is accompanied by decreased pulse pressure. Pituitrin diuresis, therefore, is due primarily to direct stimulation of the renal cells, usually aided, probably, by a concomitant vasodilatation in the kidneys.

Von den Velden<sup>2</sup> expresses a contrary view of the action of extracts of the pituitary body. He finds that these extracts depress kidney functioning, and this fact explains the benefit derived from their use in diabetes insipidus.

It is a question where the active principles of pituitrin are formed. Some authors maintain that they are derived from a colloid substance of the pars intermedia, and pass backward into the pars nervosa; while other observations indicate that the active principles are formed in the true hypophysis. Simmonds<sup>3</sup> reports the case of a woman, aged thirty-seven years, who developed an obstinate and intense polyuria. Necropsy revealed complete destruction of the true hypophysis by metastatic cancer. The author refers to Schäfer's research which established the fact that the anterior portion of the pituitary body can have nothing to do with the secretion of the urine. In Simmonds' case, the intermediate portion was intact, and he reasons that it must have been irritated to hyperfunctioning by the adjacent destructive process in the posterior portion. From this he concludes that the pars intermedia is responsible for diabetes insipidus.

Another claimed effect of pituitrin upon the organism is to increase the flow of milk, but a number of experiments have fairly well established the fact that the production of milk is not increased.

Regarding the metabolism under the influence of pituitrin, a number of observations point to increase of protein catabolism. Elfer,<sup>4</sup> from his investigations, concludes that the administration of extracts of the true hypophysis produces no ill-effects on the metabolism of proteins, and that it causes a transitory retention of phosphorus, calcium, and magnesium.

The effects of pituitrin on carbohydrate metabolism are similar to those of adrenalin, but of less degree. Injection in rabbits is followed by hyperglycemia and glycosuria. Mechanical stimulation of the true hypophysis is liable to lead to glycosuria and a decreased assimilation

<sup>1</sup> Journal of Pharmacology and Experimental Therapeutics, May, 1913.

<sup>2</sup> Berl. klin. Woch., November 10, 1913.

<sup>3</sup> Münch. med. Woch., January 21, 1913.

<sup>4</sup> Deutsch. Archiv f. klin. Med., 1913, vol. ex, Nos. 3 and 4.

of sugar. Removal of the pars nervosa stimulates the assimilation of sugar and the storing of fat.

Weed, Cushing and Jacobson<sup>1</sup> are led from experiments to conclude that the pituitary body and, more particularly, the pars nervosa, play a significant role in the metabolism of carbohydrates, and their action in this respect is under the control of fibers which reach the gland by way of the superior cervical sympathetic ganglion. Stimulation of this nervous pathway at the so-called sugar centre in the fourth ventricle, at the superior cervical ganglion, and by excitation of the hypophysis itself, liberates a chemical substance which causes glycogenolysis and glycosuria independent of any possible nervous impulse reaching the glycogen-holding cells of the muscles or abdominal viscera.

**Pituitary (Pars Anterior).** Removal of the true pituitary leads to a rapidly fatal issue. Muscular tremors, bradycardia, slowing respiration, and an antemortem fall of temperature are followed by death within a few days or weeks.

Partial removal of the true pituitary in the young inhibits growth and leads to persistence of infantile characteristics, hypertrophy of the thyroid, atrophy of the sexual glands, and increase of fat, principally in the omentum and retroperitoneal tissues.

Transplantation has been successfully carried out, with the prolongation of the life of the animal. The injection of extracts has likewise been successful in offsetting the effects of removal of the pituitary and in alleviating the symptoms of hypopituitarism.

Some investigations have pointed to an increased growth in young animals after grafting the pituitary or feeding pituitary tissues; but, other investigations agree with those of Lewis and Miller<sup>2</sup> that feeding the pituitary has no effect on the growth.

The pituitary hypertrophies during pregnancy, and this is due mainly to an increase in the chromophobe cells. Schimplert,<sup>3</sup> however, has been unable to determine any change in the hypophysis of pregnant cattle.

Castration and thyroidectomy also lead to hypertrophy of the pituitary.

Disease of the true pituitary in the young leads to giantism, while in the mature it causes acromegaly. According to Cushing, the early stages of this disease are due to an increased activity of the pituitary, while in the later stages, decreased activity supervenes.

The Fröhlich syndrome (*dystrophia adiposogenitalis*) follows partial removal of the pituitary in young animals, and is a result of decreased activity of the gland in young people. Its characteristics are chiefly arrest of development, deposits of fat, often on the buttocks and breast, and the underdevelopment of the sexual organs.

<sup>1</sup> Bulletin of Johns Hopkins Hospital, February, 1913.

<sup>2</sup> Loc. cit.

<sup>3</sup> Loc. cit.

Stetten and Rosenbloom<sup>1</sup> have carried out clinical and metabolic studies on a case of hypopituitarism of the Fröhlich type due to a cyst of the hypophysis. They found that, in this case, there was a marked perversion of some metabolic process leading to high and abnormal percentages of the neutral sulphur and undetermined nitrogen of the urine.

Cushing<sup>2</sup> advances the view that skeletal overgrowths, possibly combined with certain cutaneous changes and hypertrichosis, is an indication of anterior lobe hyperplasia. On the other hand, certain types of adiposity with an increased assimilation limit for carbohydrates, often with dry skin, subnormal temperature and pulse, are characteristic of the metabolic disturbances from posterior lobe insufficiencies. Hypotrichosis and sexual dystrophy are common accompaniments.

Assuming the combination of these factors, certain not unfamiliar clinical syndromes, in which overgrowth is associated with adiposogenital dystrophy, can be explained. They differ from the accepted syndrome of Fröhlich not only in the absence of a hypophyseal tumor with sellar enlargement, but also in their opposed skeletal features. These physical states, in brief, are interpreted as the expression of an anterior lobe hyperplasia combined either with posterior lobe hypoplasia or with what is in effect the same thing, stasis of posterior lobes excretion.

Von Bonin<sup>3</sup> says there are hardly any cases of pure hypopituitarism. Sexual infantilism and adiposity are symptoms of this condition and are generally, if not always, found associated with acromegaly—hyperpituitarism.

In discussing an interesting case of acromegaly, Grinker<sup>4</sup> says: "The peculiar distribution and extent of the tumor may explain many of the symptoms in this case. The proliferation of the glandular tissue leads one to suppose that there must also be a corresponding increase in the function of such tissue. Assuming, with Benda, Lewis and Cushing, that the skeletal overgrowth of acromegaly is conditioned by a hypersecretion of the anterior portion of the hypophysis, we certainly had the structures from which such secretions might have been derived. As the tumor continued to grow, the hyperactivity was converted into hypoactivity—the chromophil gave way to chromophobe cells. Then it was that we discovered the existence of adiposity, myasthenia, and loss of sexual power. The tumor masses consisted almost entirely of chromophobe cells, while the chromophil cells—the real secreting structure—seem to have almost entirely disappeared. Apparently there was a stage of immoderate stimulation followed by one of exhaustion. This interpretation harmonizes with the modern

<sup>1</sup> American Journal of Medical Sciences, November, 1913.

<sup>2</sup> Ibid., March, 1913, vol. cxlv, No. 3.

<sup>3</sup> Quarterly Journal of Medicine, January, 1913.

<sup>4</sup> Journal of the American Medical Association, July 26, 1913.

teaching on the causation of acromegaly. While the theory of hypophyseal activity receives but scant support from my case, more can be said under the heading of neighborhood symptoms on which Cushing in his monograph puts great emphasis. We may recall that the patient developed petit-mal attacks at first, and, as the tumor continued to grow toward the uncinate gyri, there also appeared attacks which were accompanied by a smacking of the lips and movements as though the patient were tasting some unpleasant substance. These were probably petit-mal seizures belonging to the type which Hughlings Jackson described long ago as uncinate fits—caused by the extension of the growth to the uncinate convolutions. The attacks of grand-mal epilepsy must also be considered as neighborhood symptoms. They were most probably caused by the varying fluid-content in the ventricles compressing the brain against the skull, thus producing cortical irritation. To the invasion of the frontal lobe by the tumor must be attributed the mental changes, somnolency and puerile behavior—symptoms frequently noted in acromegaly. The absence of visual disturbances in my case can be explained from the appearance of the optic chiasm. The chiasm appears thinned out, but widened; evidently the neoplasm compressed this structure very slowly, thus permitting gradual accommodation to pressure, while the tumor itself showed tendency to extend laterally, rather than to grow in an upward direction.

"A symptom which may throw some additional light, as every such case must, on the interrelationship existing between the various glands of internal secretion, was the complete absence of a thyroid gland in my patient. Possibly in taking up the work of the thyroid, the hypophysis continued to grow and functionate beyond the physiologic needs, with the resulting formation of a large adenoma."

Bartlett<sup>1</sup> describes a case of acromegaly with a polyglandular syndrome. This syndrome is represented by (1) a chromophil cell adenoma of the anterior lobe of the hypophysis, (2) a persistent and non-involved thymus, (3) a colloid goitre with marked desquamation of the parenchymatous cells, (4) hypertrophy of the chromaffin cells of the adrenal medulla, (5) hyperplasia of the endothelial elements of the lymph nodes and of the spleen, (6) enlargement of the pineal body, and (7) atrophy of the cells of Sertoli and of Leyding (assumed on the basis of the loss of sexual function, and from other similar case reports).

**The Chromaffin System.** The chromaffin tissue made up of cells which have a peculiar affinity for chrome salts, staining a distinct brownish color, forms the medulla of the suprarenal bodies. The cortex of these bodies consists of an entirely distinct tissue, the interrenal tissue. It has been difficult to investigate the physiology of these two tissues because of their close physical association. However, some distinct advances in our knowledge of them have been made.

<sup>1</sup> Archives of Internal Medicine, August, 1913.

The active principle obtained from the adrenal glands is known as adrenalin, and, chemically, it is orthodioxyphenyl-ethanol-methylamine. Although it is closely related to tyrosin, a decomposition product of protein, it is a true physiological secretion and not a postmortem product. It has been shown that when the splanchnic nerves supplying the suprarenal bodies are stimulated, there results an increase in the amount of adrenalin in the blood of the vein leaving the gland.

Numerous tests for adrenalin have been described which depend chiefly upon the fact that it is readily oxidized to oxyadrenalin, which imparts a red color to its solutions. Seidell<sup>1</sup> calls attention to defects of previous methods and proposes a new colorimetric test which consists in the use of manganese dioxide as the reagent for developing a color with aqueous epinephrin solutions or suprarenal gland extracts. The color so developed is estimated by comparison with artificial color standards made by mixing cobalt chloride, gold chloride and water.

The most prominent action of adrenalin is upon the vascular system where it causes a marked rise of blood-pressure through constriction of the arterioles and a slowing of the heart.

Vessels of different regions react differently to adrenalin. The splanchnic vessels give the greatest response, and the renal arterioles are the first to be constricted and are the ones which respond to the smallest dose. The intracranial and pulmonary vessels are but slightly acted upon, while the coronary arteries are dilated instead of constricted. Meyer,<sup>2</sup> in experiments on dogs and cats, has confirmed the finding that epinephrin dilates the coronary vessels. It has been found that this active principle stimulates both motor and inhibitory terminations of the true sympathetic, and its vasoconstrictor action is due to the preponderating action of constrictor endings in the sympathetic nerves. Where these constrictor fibers are absent, as in the coronary arteries, adrenalin causes dilatation.

When the vagi are intact, adrenalin produces a slowing of the heart, but when these nerves are cut out by atropine, the effect on the heart is that of acceleration. The inhibitory action is probably produced by a reflex through the vagus from increased arterial pressure. It has been determined that the acceleration occurring when the vagi are cut out is due to the action of epinephrin on the terminations of the augmentor nerves.

*Throughout the organism, adrenalin produces the same effects as stimulation of the true sympathetic.* In the alimentary canal, it inhibits peristaltic movement and causes contraction of the pyloric and the ileocecal sphincters. It stimulates contraction in the reproductive organs, and causes dilatation of the pupil if the influence of the superior cervical ganglion is cut out.

<sup>1</sup> Journal of Biological Chemistry, Baltimore, August, 1913.

<sup>2</sup> Berl. klin. Woch., May 19, 1913.

The subcutaneous or intravenous administration of adrenalin causes marked changes in metabolism. It leads to a glycosuria, with hyperglycemia, and is accompanied by an increased excretion of nitrogen, showing increased catabolism of proteins. It has been found that, after repeated administration of adrenalin, considerable quantities of glycogen or even an accumulation of this substance is present. This may indicate that the production of sugar from proteins has been so great as to leave a surplus available for storage.

The finding that adrenalin increases the sugar-content of the blood in dogs from which the pancreas has been removed leads to the view that its action in the production of hyperglycemia is not one upon the pancreas alone, and suggests the thought that the inhibiting influence of the pancreas and the stimulative influence of adrenalin act at some common point, and in view of the law that the action of adrenalin is similar to stimulation of the true sympathetic, this common point may be the termination of the true sympathetic in the liver. This possibility is further strengthened by the finding that stimulation of the hepatic plexus produces a glycogenolysis.

Facts have been adduced which favor the idea that puncture diabetes is produced through central stimulation propagated down the splanchnics to the suprarenal bodies, causing an increase in the output of adrenalin.

The observation that in adrenalin glycosuria in ducks the respiratory quotient is increased, indicating that the tissues are using sugar, tends to differentiate the condition of adrenalin glycosuria from that of pancreatic diabetes.

Estimates of the amount of adrenalin in the blood show a proportion of about 1 in 500,000,000, and numerous observations lead to the conclusion that this is too small an amount to produce any physiological effect on the vascular system.

Some investigators look upon the relationship between this secretion and the sympathetic system as merely a means of promoting muscular efficiency in times of stress.

Ordinarily, the amount of adrenalin in the blood is so small that its action would seem better explained as an activator, rather than as a direct stimulator.

Noel Paton says that "the evidence seems to show that the initial effect of any activity of the autonomic system is apart from the influence of adrenalin, but that if the action is to be sustained, it is accompanied by an outpouring of adrenalin which must fortify the nervous effect either by making the nerve endings more sensitive—by activating—or by replacing and superseding this effect—by directly stimulating. The fact that the nervous effects under normal conditions remain definite and limited, tells against the latter hypothesis."

Adrenalin in large dose may lead to cardiac inhibition and rapid death.

Where the poisoning is more chronic, liver necrosis has been noted, while continuous administration of this active principle leads to atheromatous changes in the vessels, as noted by numerous observers.

**The Interrenal Tissue.** The interrenal tissue makes up the cortex of the suprarenal bodies and is distinct in origin, character, and probably in function from the adrenal or chromaffin tissue. As noted before, the close physical relationship of these two tissues has rendered study of their physiology most difficult. In the lower fishes, however, the interrenal bodies are quite separate from the adrenals, and Biedl has taken advantage of this fact to study the effects of removal. His experiments indicate that whatever influence may be exerted by the adrenal bodies on the organism, the interrenal bodies are essential in the maintenance of life. He found that animals from which they were removed gradually became weaker, refused food, and finally died in from fourteen to eighteen days.

The results of transplantation of these structures, and of the injection of their extracts, have led to no definite conclusions.

A notable paper by Glynn on "The Adrenal Cortex, its Rests and Tumors, together with its Relation to Other Ductless Glands, and its Relation to Sex," was reviewed in these pages last year.

Recently Voegtl<sup>1</sup>lin and Macht<sup>2</sup> have succeeded in isolating a crystalline principle from both the blood and adrenal cortex of the ox which acts as a vasoconstrictor on the vessels of frogs and rabbits, and has a digitalis-like action on the frog's and mammalian heart.

In discussing the morbid functioning of the suprarenals, Bernard<sup>2</sup> calls the adrenal syndromes respectively, *hyperepinephria* and *hypoepinephria*; the former is characterized by abnormally high arterial blood-pressure, atheroma of the aorta, and glycosuria, although each of these may have causes apart from adrenal functioning. Hypoepinephria is characterized by weakness of the muscles and abnormally low blood-pressure; the latter entails various circulatory disturbances, tachycardia, arrhythmia, tendency to collapse and syncope, and peripheral vasomotor disturbances. In addition to these, the hypo-epinephria may entail digestive disturbances, especially vomiting, and nervous disturbances, including mydriasis, headache, delirium, convulsions or apoplectiform attacks and coma, or even sudden death in some cases. This insufficiency may be acute, subacute or chronic. Bernard thinks that abnormal pigmentation is due to nervous influences; when the pigmentation is accompanied by symptoms of hypo-epinephria, the syndrome of Addison's disease results.

The relations of Addison's disease to the suprarenal bodies are by no means clear. Noel Paton says that "the muscular weakness and emaciation are probably similar to the condition produced in lower

<sup>1</sup> Journal of American Medical Association, December 13, 1913.

<sup>2</sup> Presse m<sup>é</sup>dical<sup>e</sup>, Paris, October 4, 1913.

animals on removal of the suprarenals, and if these are to be associated with loss of cortex, as indicated by Biedl's experiments on the skate; we should be inclined to refer the symptoms to loss of cortex from the tubercular lesion. The postmortem reports on cases are far from satisfactory, some observers describing destruction of the cortex; others, of the medulla; most of both. There seems little evidence that the loss of medulla has any causal relations to the symptoms, for there is no evidence that adrenalin exercises any tonic effect upon skeletal muscle."

Referring to the adrenal muscle syndromes, Sezary<sup>1</sup> finds that, besides Addison's disease, there are several other conditions of extreme muscular debility which recent research is connecting with insufficiency of adrenal function. Among them is the myasthenia of Erb-Goldflam. His experience demonstrates that certain slow changes in the adrenals, alone or with changes in other ductless glands, may induce a myasthenic syndrome impossible to distinguish clinically from myasthenia independent of adrenal functioning. It has been shown that amyotrophy may occur from defective adrenal functioning. This is particularly liable in chronic disease, and we may thus link diffuse amyotrophy with wasting diseases through the intermediation of the adrenals. Laboratory research has demonstrated that epinephrin is utilized by the muscle in contraction. Consequently, the lack of adrenal secretion deprives the muscle to an extent of its power to contract. On the other hand, an excess of adrenalin is liable to cause hypertonicity in the muscle, and this may account for permanent contraction in some cases.

Arterial pressure is the result of two distinct forces: the energy of the heart impulse, and the sum total of the peripheral resistance. Each of these forces is more or less under the control of the adrenal secretion. In its vasoconstrictor action it increases, by its excess, or reduces by its deficiency, the peripheral resistances. At the same time, by its parallel action on muscle tissue, it reenforces or weakens the energy of the cardiac impulse; thus with adrenal insufficiency the arterial pressure sinks, and with excessive functioning this pressure rises. Josué has made a special study of this form, calling it the adrenal-vascular syndrome. Its main elements are excessive adrenal secretion, hypertrophy of the heart, and arteriosclerosis. This type is a special form of the adrenal muscle syndrome.

Hoke<sup>2</sup> reports a case of peculiar asthenia in a woman, aged thirty-two years, who had never been quite healthy since an attack of diphtheria at fourteen. She tired easily, had palpitations, dizziness, and sudden sweating on slight exertion. On being called to see the patient, he found the skin pallid and clammy, the pulse scarcely perceptible, the

<sup>1</sup> Semaine médicale, February 5, 1913.

<sup>2</sup> Wien. klin. Woch., October 2, 1913.

heart rate 52 and regular, the heart sounds pure, and the temperature 35.8 C. by the mouth. The patient felt that she was dying. On administering 0.5 c.c. of 1 to 1000 adrenalin solution, the effect was surprising. In fifteen minutes the patient felt well and strong with a good pulse of 62. She was then given a course of carbonated baths, and now seems to be permanently improved. The myasthenia is much better, the pulse 72, and the systolic pressure 110.

Terrien<sup>1</sup> calls attention to a condition of periodic vomiting in children which is probably of adrenal origin. These attacks are accompanied by acetonemia, as discovered through the breath, and by pallor, small rapid pulse, and apathy. In one case, the child complained of pain in the abdomen and limbs without exact localization, and this child died suddenly as it made a slight effort. In the other two cases which he describes, the administration of epinephrin ended the attacks. The features of the cyclic vomiting which suggest the participation of the adrenals are in particular the marked asthenia from the first, the "white line," and the tendency to sudden death.

**The Reproductive Glands.** The influence of the reproductive glands upon the organism is profound, and there is abundant evidence that this influence is exerted through an internal secretion. In the male, there are numerous examples of the results of castration. If this condition is produced in the young, the male sex characters do not develop. Striking illustrations of this are found throughout the animal kingdom. Stags, if castrated young, do not develop antlers. If castration is performed at the time the antlers should grow, these are abortive in form; and, following castration, when the horns are developed, the animals shed the antlers and abortive ones take their place. In the eland, both sexes possess horns, and here castration does not affect their growth in the male. Destruction of the testes in the spider crab leads to the development of egg-bearing abdominal appendages. The influence of the sexual glands on the organism is well shown in cases of pubertas precox. Their influence is also shown through the effects of transplantation and the administration of extracts. Smith and Crocker<sup>2</sup> have carried out a series of experiments on old hens with observations extending over a year. To these animals they gave frequently injections of salt solution extracts of testes, and, in the course of their observations, the animals showed distinct development of male characters. The combs became much larger and brighter. The neck feathers became more brilliant, the small tail feathers showed some growth and more brilliance. In one hen there occurred a distinct growth of spurs. The production of eggs diminished, and was finally abolished. In many of the animals a spirit of combativeness developed, as well as male sexual instincts. In all probability, the secretion which

<sup>1</sup> Bull. de la Soc. de pediatrie, February, 1913.

<sup>2</sup> New York Medical Journal, July 5, 1913.

exerts this profound influence on the structure and functions of the organism is produced by the interstitial cells of the testes. These cells are very similar in origin and character to the cells of the interrenal tissue, and Glynn<sup>1</sup> has shown what a profound influence this tissue exerts on the sex characters.

In the female, the effects of removal of the sexual glands are not so abundantly illustrated as in the case of the male. When the ovary is diseased or removed, somatic changes are likely to occur which tend to the acquirement of opposite sex characters. Cases of pubertas precox illustrate the effect of the sexual glands on the organism in the female as well as in the male. Transplantation experiments afford striking evidence of the influence exerted by the ovaries on the organism. The grafting of these glands into young castrated male rats has led to the development of many female sex characters, and it has been found that the interstitial cells of the ovary are alone sufficient to bring about these results.

A number of observations show that the ovaries, or corpora lutea, have a pronounced influence upon the uterus in preparation for pregnancy. These glands likewise influence the development of the mammae. Cohn,<sup>2</sup> from animal experiments and his observation of human cases, concludes that the internal secretion of the ovary exercises a stimulating effect on the growth of the mammary gland, but has an inhibitory influence upon the milk secretion.

The condition of estrus in both the male and female is determined by the gonads. The gonads unquestionably exert an influence on the metabolism, but the investigations along this line have been unsatisfactory and not at all convincing.

**The Pancreas.** The pancreas is primarily a digestive gland, but, in addition to its function as such, it exerts an influence on the metabolism, probably through the action of an internal secretion. The removal of this gland from animals throughout the vertebrate kingdom leads to a condition of true diabetes. If a portion of the gland is allowed to remain, one-third or even one-fifth, diabetic symptoms do not develop. That its influence is not exerted through the nervous system, but in all probability by means of an internal secretion, has been proved by transplanting a piece of the gland and thus preventing the diabetic condition. If this graft be subsequently removed, diabetes results.

The administration of pancreatic extracts seems to have no influence in the prevention of diabetes. Murlin and Kramer<sup>3</sup> have shown that neither the extract of pancreas alone nor the double extract of pancreas and duodenal mucosa has any effect on the respiratory quotient in depancreatized dogs. This shows that these measures are of no importance in restoring to the depancreatized dog the ability to burn sugar.

<sup>1</sup> Loc. cit.

<sup>2</sup> Monatsschrift f. Geburtshilfe und Gynäk., January, 1913.

<sup>3</sup> Journal of Biological Chemistry, August, 1913.

The action of the pancreas on carbohydrate metabolism is probably a double one, checking the mobilization of sugar in the liver, and facilitating its utilization in the tissues. For a discussion of the influence of the pancreas on carbohydrate metabolism the reader is referred to the section on Diabetes.

**The Intestinal Mucosa.** From the mucosa of the upper portion of the small intestine a substance has been extracted which, when injected into the circulation, causes an increase in the secretion of pancreatic juice, as well as an increase in the flow of bile. This extract is known as *secretin*.

The interrelationships of the ductless glands are not easy to define, although facts adduced point clearly to close relationships between certain of these glands, and it is not at all improbable that all of them are indirectly related. A relationship seems to be established through their source of origin. Thus, the chromaffin tissue and the hypophysis arise from the nervous system, and the extracts of these two tissues have a more or less similar action. The thyroid and pituitary arise from the buccal cavity, and there is apparently a close relationship between these two glands. The parathyroids and thymus develop as epithelial outgrowths from the branchial arches, and there is some evidence which points to a supplementary or compensatory relationship here. The reproductive glands and the interrenal bodies take origin from the mesothelium of the genital ridge, and the influence which these two tissues have upon the development of sex characters shows a close relationship between them. The pancreas and mucosa of the small intestine arise from the gut tract, and here is shown a relation between the secretin of the mucosa and the pancreas in the stimulation of the latter by the former.

The relationship of the thyroid to the pituitary seems to be close. These two structures apparently constitute a check upon each other. Hypertrophy of the pituitary follows thyroidectomy, and hypertrophy of the thyroid follows excision of the pituitary. Their influences upon the somatic structures is very evident. Decreased activity of the thyroid leads to underdevelopment of the bony structures and to pronounced changes in other tissues, especially the skin and its underlying structures; while increased activity of the pituitary leads to excessive growth of the bones and connective tissues.

Some observers have taken the ground that in the insufficiency of the thyroid gland its function is vicariously taken up by the pituitary, but this view has met with contention.

In regard to the relationship of the thyroid gland with the parathyroid bodies, no definite conclusion can be drawn. While a functional and even a morphological relationship is contended by some authors, the majority seem to hold that these glands are quite distinct, both morphologically and physiologically. The action of the parathyroid glands

upon the nervous system is somewhat similar to that of the thymus, and in this respect they would be antagonistic to the thyroid. If an adequate amount of parathyroid tissue be left *in situ* and the thyroid gland removed, it has been observed that there is an increased tolerance for glucose, while this tolerance is decreased if all of the parathyroid tissue be removed. This fact also points to antagonism between these glands.

Morphological studies have been made which show that on removal of the thyroid a change in the structure of the parathyroid tissue occurred which rendered it difficult to distinguish from thyroid tissue.

The relationship of the thyroid to the thymus is not at all clear. There have been contradictory findings in regard to this relationship. Basch,<sup>1</sup> who has worked so extensively on the thymus says that this organ stands in the nearest relationship to the thyroid, both pathologically and in the history of its development. They both belong to the group of branchiogenous organs, and their relationship is brought out through their similar functional relations to the bony system, the nervous system and the pupillary apparatus of the eye. The participation of the thymus in Graves' disease is of a secondary nature. It is apparently called forth by an early disturbance and enlargement of the thyroid which leads to a synonymous enlargement of the thymus.

In considering the relation of the thyroid to the reproductive glands, we find that both stimulate growth, but in different ways. Removal of the thyroid inhibits the growth of the gonads. On the other hand, castration seems to have little effect on the thyroid. The increase in the size of the thyroid during menstruation points to a relation of some kind between these glands.

Practically nothing is known regarding the interaction of the hypophysis and the thyroid.

The fact that hyperthyroidism is often accompanied by glycosuria suggests a relation between the thyroid and the pancreas. This relationship, however, may be through the adrenals, which are stimulated by the thyroid and in turn inhibit the action of the pancreas through stimulation of the hepatic plexus.

In considering the relationships of the gonads to the other ductless glands, we find that while the pituitary stimulates the gonads, these glands inhibit the pituitary. Both exert a similar influence upon growth, promoting especially the growth of the long bones. The thymus supplements the action of the testes, and, while both stimulate growth and development, each inhibits the growth of the other. The relationship of the gonads to the interrenals is plainly shown in their similar action on the development of sex characters.

The relations of the chromaffin system are principally with the thyroid and pancreas. The thyroid stimulates the chromaffin tissues,

<sup>1</sup> Ztschr. f. exper. Path. u. Therap., 1913, xii, 2.

but there seems to be no action in the opposite direction. Hypothyroidism leads to a decreased output of adrenalin, while hyperthyroidism leads to hyperadrenalinemia. The chromaffin system inhibits the action of the pancreas in its inhibition of the mobilization of sugar, but there is apparently no action in the other direction.

Knowledge of the relationships of the parathyroids to the other ductless glands is slight. No definite relation between these glands and the gonads has been established, but some facts may possibly suggest a relationship. The parathyroids and thymus have a common origin, and in all probability there exists a physiological relation between these glands. Some observations have shown that removal of the thymus produces nervous symptoms similar to those following parathyroidectomy.

## OPHTHALMOLOGY.

By EDWARD JACKSON, M.D.

**Use of the Ophthalmoscope.** The ophthalmoscope is used under such conditions that a perfectly made instrument is not merely easier to use, it enables the observer to see appearances that would escape notice with an instrument even slightly defective. Marple<sup>1</sup> emphasizes the need for a perfect instrument in describing his latest electric ophthalmoscope. A well-made *electric ophthalmoscope* reduces enormously the principal difficulties of ophthalmoscopy, namely, the keeping of the light properly directed into the eye, and the annoyances of the corneal reflexes. Elliot<sup>2</sup> thinks that it is one of the greatest recent advances in the armamentarium for ophthalmic diagnosis. But he points out that in an excessively damp climate the patient and surgeon are liable to annoyance from a slight electric shock, unless especial precautions are taken to secure insulation. Gifford<sup>3</sup> calls attention to the value of throwing the edge of the light area on the part of the retina to be examined, to bring out slight retinal changes, that might escape notice under strong illumination.

### DISEASES OF THE CONJUNCTIVA.

**Temperature of the Conjunctiva.** Howe<sup>4</sup> has applied the thermocouple to measure differences between the temperature of the conjunctiva and that of the mouth. With this instrument, a difference of 0.03 degree Centigrade, or less, is certainly indicated. He finds that, normally, the conjunctiva back of the inner or outer canthus is 0.3 to 0.4 degree lower than that of the mouth, and that it is 0.1 degree lower immediately over the cornea than at the inner or outer canthus. Pledgets of cotton moistened with ice-water and applied over the lids in rapid succession, reduce the temperature of the conjunctiva from 1° to 1.5° C. in four or five minutes. But it cannot in this way be reduced much lower.

**Circulation in Conjunctival Vessels.** The binocular corneal microscope capable of magnifying from 20 to 100 diameters, makes it possible to see the movement of the blood-corpuscles in the conjunctival capillaries,

<sup>1</sup> Ophthalmoscope, vol. xi, p. 663.

<sup>2</sup> Ibid., p. 145.

<sup>3</sup> Ibid., p. 193.

<sup>4</sup> Section on Ophthalmology, American Medical Association, 1913, p. 249.

under perfectly normal conditions. Luedde<sup>1</sup> points out this is of greater practical value than studying the circulation in the web of the frog's foot, or the exposed mesentery. Changes in the retinal vessels can only be seen and appreciated by the expert ophthalmoscopist. But the conjunctival vessels may be studied by any one accustomed to use the microscope. He finds that in *angiosclerosis* these changes are demonstrable as soon as the lumen of the vessel begins to be encroached upon. The normal vessels are tortuous, but free from sharp angles which appear with pathologic changes. Saccular or fusiform dilatations occur in the small arteries, and have the same significance as in larger vessels.

**Ophthalmia Neonatorum.** The compulsory reporting of this disease in London seems to show that it occurs there in 0.843 of 1 per cent. of reported births, while, of the children affected, only 5.6 per cent. showed any permanent damage to the sight, and one-half of these children retained one undamaged eye. Harman,<sup>2</sup> who calls attention to these facts, holds that the indiscriminate application of strong antiseptics to the eyes of all newly born infants is unwarranted. He urges attention to any vaginal discharge before delivery; and the careful cleansing of the eyes immediately after birth. Cheney<sup>3</sup> urges that each case should be promptly placed under the supervision of an oculist; and that literature with reference to the prevention of ophthalmia neonatorum should be sent to each physician every three or six months for the next ten years. Holloway<sup>4</sup> would make it mandatory to report all births within twelve hours, and upon receipt of this report, to supply the parents with printed instructions. A measure also advocated by Cheney.

Mittendorf<sup>5</sup> reports satisfactory results in 8 cases of gonorrhreal conjunctivitis treated with *gonococcal vaccines*, but does not advise dependence upon this to the exclusion of local treatment.

**Trachoma.** The relation of the *cell inclusions* found in trachoma, so-called trachoma bodies, to trachoma still remains unsettled. Inoculation of the conjunctiva in apes seems to indicate that they probably cause the disease. But, on the other hand, the finding of such cell inclusions apart from trachoma inclines most observers to think they are not the cause. Lindner<sup>6</sup> holds to the former view. Cohen<sup>7</sup> believes that the inclusion bodies do not belong to trachoma, but to an independent conjunctival affection. Harrison<sup>8</sup> has found only one band of three hundred Indians in the United States not affected with trachoma.

<sup>1</sup> American Journal of Ophthalmology, vol. xxx, p. 129.

<sup>2</sup> British Medical Journal, May 24, 1913.

<sup>3</sup> Boston Medical and Surgical Journal, vol. clviii, p. 117.

<sup>4</sup> Ophthalmic Record, vol. xxii, p. 717.

<sup>5</sup> Medical Record, vol. lxxxiii, p. 428.

<sup>6</sup> Graefe's Archiv für Ophthalmologie, vol. lxxxiv, p. 1.

<sup>7</sup> Archives of Ophthalmology, vol. xlvi, p. 29.

<sup>8</sup> Ophthalmic Record, vol. xxii, p. 649.

Wibo<sup>1</sup> has used *carbon dioxide snow* for the destruction of the trachoma granules, and reports that with it the granule is destroyed in fifteen to twenty seconds, almost without pain, with perfect asepsis, and with a very low cost per patient. He thinks it possible, by this treatment, to cut short epidemics in schools, barracks, etc. The snow is applied in the form of a crayon, the point of which is pressed against the conjunctiva for fifteen or twenty seconds and the lid is afterward kept everted double that time. From two to ten points are touched at a single sitting. Frictions with sublimate were also used to supplement this treatment. As none of the cases had been under observation six months after subjection to this treatment, further studies will be needed to indicate the permanence of the good results.

**Parinaud's Conjunctivitis.** The tendency of this disease to run a regular limited course, after beginning with chills and pyrexia, with definite symptoms involving one eye and its related lymph glands, has marked it as a distinct clinical entity. But efforts to discover the specific cause have been unsuccessful, until within the last year Verhoeff<sup>2</sup> has recognized a specific microorganism resembling a *leptothrix*, forming filamentous masses from 10 to 60 micra in diameter. Each mass was surrounded by an area of cell necrosis, such as he had previously recognized as characteristic of the disease. The threads are about the thickness of an influenza bacillus. They contain dots which may be separated by spaces three or four times the thickness, or scattered at longer intervals. After recognizing this organism, Verhoeff examined sections from 11 other cases, finding it present in all but one. It can be brought out by staining with carbol-thionin, but is best differentiated in tissue fixed with Zenker's fluid, and stained by the Gram method, after preliminary treatment of the sections with xylol-balsam. Several observers have found that cases clinically thought to resemble Parinaud's conjunctivitis showed evidence of tuberculous infection of the conjunctiva. Two cases of the kind have been reported by Rosenhauch,<sup>3</sup> and one by Mellinger.<sup>4</sup> The former believes that this form of conjunctivitis may arise from different causes. But Verhoeff's demonstrations suggest that inaccurate diagnosis has caused this confusion.

#### CORNEA AND SCLERA.

**Action of Quinine and its Derivatives on the Cornea.** Quinine was used in collyria for conjunctivitis and corneal ulcers more than thirty years ago. But, in part on account of the irritation caused by acidity

<sup>1</sup> Annales d'Oeulistique, vol. exlix, p. 172.

<sup>2</sup> Archives of Ophthalmology, vol. xlvi, p. 325.

<sup>3</sup> Archiv für Augenheilkunde, vol. lxxii, p. 162.

<sup>4</sup> Archives d'Ophtalmologie, vol. xxxiii, p. 524.

of the salts employed, and because of the exploitation of newer chemical compounds, its value has been lost sight of. One of its recent derivatives, *ethylhydrocuprein*, comes to the front as a *corneal anesthetic*, and as a *specific for pneumococcus ulcer* of the cornea. Morgenroth<sup>1</sup> and Ginsberg<sup>2</sup> and Kaufmann, experimenting on the eyes of rabbits, found that with the above drug, or with the alkaloid quinine dissolved in olive oil, a 1 per cent. solution diminishes the sensibility of the cornea, and a 2 to 4 per cent. solution produces complete anesthesia lasting from ten minutes to an hour. And with a 4 per cent. solution anesthesia continued even four days; but with a clouding of the cornea that had not entirely cleared up in eight days.

Ginsberg and Kaufmann experimented by infecting both corneas of the rabbit with the pneumococcus, and treating one eye with the quinine alkaloid, usually the ethylhydrocuprein. Then an emulsion of each cornea was injected into mice. Of the corneas treated by subconjunctival injections of the quinine salt, two-thirds were sterile after three to six hours' treatment. But the control corneas always showed the germs still virulent. Goldschmidt and Schur<sup>3</sup> were led, by these experiments, to try ethylhydrocuprein in the treatment of pneumococcus ulcer, and they report remarkably favorable results. Goldschmidt also reports 22 cases. Of these, the cornea was perforated in four, three of which were advanced cases ready to perforate when the treatment began. All cases treated early were promptly cured.

Goldschmidt's method of application was by the instillation every hour, of a 1 per cent. or 2 per cent. solution. Schur prefers the application of a pledget of cotton, soaked in a 2 per cent. solution, directly to the surface of the ulcer for a period of five or ten minutes. This causes at first a sharp burning, that may be diminished by previous use of a local anesthetic. It may be repeated, if necessary, at intervals of three hours. The application is followed by some haziness of the cornea surrounding the ulcer. In a case reported by Darier,<sup>4</sup> this required fifteen days to clear entirely. In his 2 cases, Darier, however, applied a minute particle of the powder to the cornea, causing severe burning pain which lasted for some hours.

**Heat for Corneal Ulcers.** Weekers<sup>5</sup> bases his method of treatment for infected corneal ulcers on the fact that the pneumococcus, and the diplobacillus of Morax-Axenfeld, are killed by a temperature of 55° C. in five minutes, or instantly at a temperature of 65° to 70° C. He used the galvanocautery tip heated to almost white heat, and held close to the ulcer for one minute, without actually touching it. The surface

<sup>1</sup> Centralblatt für praktische Augenheilkunde, vol. xxxvii, p. 315.

<sup>2</sup> Klinische Monatsblätter für Augenheilkunde, June, 1913, p. 804.

<sup>3</sup> Ibid., October to November, 1913, p. 450, 469.

<sup>4</sup> Clinique Ophthalmologique, vol. xx, p. 17.

<sup>5</sup> Archives d'Ophthalmologie, vol. xxxiii, p. 681.

becomes white and dry. He waits until it gets moist again then repeats the exposure for the same time, and sometimes makes even a third application of the kind. He reports the results obtained by this method in 47 cases of severe progressive corneal ulcer. No eye was lost. Two retained light projection; fifteen could count fingers; thirteen had vision of 5/60; and in seventeen it varied from 5/36 to 5/9.

**Phlyctenular Ophthalmia and Episcleritis.** From a general review of the subject, Will Walter<sup>1</sup> concludes that these diseases are due to the associated action of tuberculous infection and malnutrition. He thinks the treatment by excluding from the dietary cane sugar, acids, tea, coffee, sterilization of the intestinal tract by calomel, continued many days, with fresh air, and a nourishing, bland diet, or an "alkaline dietary," is a good basis for the modern immunizing treatment. In the specific therapy he insists that the doses of *tuberculin* should be so small as to produce no appreciable reaction beyond an increase in the leukocytes. He confesses the difficulty in restraining oneself from obtaining a visible reaction. But one is repaid by the results.

**Keratoconus.** Weeks,<sup>2</sup> who reports 14 cases of conical cornea, gives a general review of the diagnosis and treatment. In the beginning it is difficult to recognize. The altered and irregular refraction gives the first evidence. This may be studied with the ophthalmoscope, by skiascopy, or with the ophthalmometer, or Placido's disk. Such early cases are to be treated by the best correction of their astigmatism and myopia, with attention to any departure from general health, and prolonged use of pilocarpin in the eye. When vision has fallen to 8/200 or less, it may be improved very much by operative procedures. These should reduce the tension of the eye as much as possible, and maintain the reduction for a long period of time, until the healing is complete and the cicatrices firm. To this end he has done iridectomy, placing the coloboma where it would be of greatest aid to vision. Ten days later he has cauterized the apex of the cone with a platinum point, heated to redness in the flame of a spirit lamp; making the eschar as deep as possible without perforating the cornea. After this a compress bandage with borated vaselin was applied continuously for three weeks, and at night for two months. Pilocarpin was continued during this period.

**Wounds of the Sclera.** How best to deal with these may puzzle the specialist, as well as the general practitioner who is likely to be called first in such an emergency. Francis<sup>3</sup> has employed the reinforcement of the injured coat by conjunctival tissue, by means of a double conjunctival flap. He thinks if the conjunctiva can be made to exert enough traction on the wound margins to bring and hold them together

<sup>1</sup> Section on Ophthalmology, American Medical Association, 1913, p. 215.

<sup>2</sup> American Ophthalmological Society, vol. xiii, p. 293.

<sup>3</sup> Section on Ophthalmology, American Medical Association, 1913, p. 407.

while reinforcing the injured coat, the more difficult and less desirable scleral suture may be avoided. His operation is suited to wounds far enough back from the corneal limbus to permit free elevation of the neighboring conjunctiva on all sides.

The conjunctiva is freely loosened with a strabismus hook, for a space extending about one-quarter of the circumference of the eyeball. Double-armed, fine silk sutures are placed in the margin of one conjunctival flap. The needles are then carried under the other flap well away from the wound, brought out to the conjunctival surface, and the suture firmly tied. This tucks the first flap under the other, covering the scleral wound with one layer of conjunctiva. The surface is then abraded by gentle scraping with a knife, then the other flap is brought over the first and stitched down in the opposite direction. The suture must be snugly drawn and firmly knotted, otherwise there will not be sufficient traction to hold the scleral edges closely together. If the wound is such that the conjunctival flap cannot be wholly trusted, one or more scleral sutures of very fine catgut, or kangaroo, or rat-tail tendon, may first be placed in the sclera. Francis finds that this operation gives a thick, firm, unyielding scar, while the two layers of sound conjunctiva protect the contents of the globe from outside infection.

#### ANTERIOR CHAMBER, PUPIL, AND UVEAL TRACT.

**Coagulation of Aqueous Humor.** Barraquer<sup>1</sup> did a preliminary iridectomy on the left eye in a case of cataract. Healing was normal, but on the third day he found the anterior chamber filled with a bluish-white substance hiding the pupil and iris except at the periphery. After a month the anterior chamber rapidly cleared up. Three years later the cataract was extracted without accident, and giving ordinarily good vision. At the end of a week of normal healing, the anterior chamber again filled with an opaque grayish-white substance, which hid the pupil and iris. This disappeared two days later, after a subconjunctival injection of sodium chloride, 2 per cent. Three years before coming to Barraquer, the right eye had been operated on for cataract by de Weeker, and on the fourth day lost all vision and presented a similar white appearance which continued about a month, and cleared up entirely. The patient obtained good vision in both eyes.

Terrien and Dantrelle<sup>2</sup> have studied, experimentally, the coagulability of the aqueous. They find that in the rabbit the normal aqueous does not coagulate. But if the anterior chamber is again opened five minutes after the first puncture, the fluid obtained promptly coagulates. Some coagulability was also developed by use of silver nitrate or mercury

<sup>1</sup> La Clinique Ophtalmologique, vol. xix, p. 79.

<sup>2</sup> Archives d'Ophtalmologie, vol. xxxiii, p. 607.

oxycyanide in the conjunctival sac, or by introducing foreign bodies into the anterior chamber. The presence of a soluble calcium salt seems necessary to coagulation.

**Pupil Reactions.** The view of Heddaeus and Hess that the pupillo-motor region of the retina is confined to a relatively small area, has been confirmed by the experiments and clinical studies of Walker.<sup>1</sup> This restriction of the area to a region near the fixation-point limits the applicability of the *hemianopic pupil reaction of Wernicke*. Probably no reliable test for the hemianopic reaction can be made without special apparatus. It explains the contradictory results that have obtained in attempting to bring out this reaction and indicates that its clinical value, in revealing if a lesion causing hemianopsia is peripheral to the primary optic centres or not, is very restricted.

**Inequality of Pupils in Pulmonary Disease.** Bukolt<sup>2</sup> found among thirty-five patients with unilateral pneumonia, that twenty-three had inequality of the pupils; the pupil on the affected side being the larger in fourteen, and smaller in nine cases. In seventeen cases in which the pneumonia was complicated by pleurisy, sixteen presented unequal pupils, ten being the larger, and six the smaller on the affected side. Including various forms of pleurisy and tuberculosis, ninety-four patients were examined for such inequality, of whom sixty-five showed anisocoria. In thirty-nine the mydriasis, and in twenty-six the miosis, was on the affected side. This rather extended study indicates that inequality of the pupils is not reliable as a sign of the side of the pulmonary lesion in any doubtful case.

**Causes of Uveitis.** *Iritis* is the most serious ocular inflammation that the general practitioner undertakes to treat. In most cases the ciliary body or choroid, or both, are involved. There is great need that these cases should be thoroughly understood by the family physician. Except when due to local infection, as through injury or corneal ulcer, cases of uveitis are caused by general conditions, or disease remote from the eye. The pathogenesis of chronic uveitis, excluding the syphilitic, tuberculous, and sympathetic varieties, was the subject of a report by de Schweinitz,<sup>3</sup> to the Seventeenth International Congress of Medicine. His report is based on the recent literature of the subject, a collection of the views and experiences of American colleagues, and a study of so-called gastro-intestinal "auto-intoxication" in relation to these affections. He holds that probably every case of uveitis is of septic or toxic origin.

Iritis has often been called rheumatic but any connection of iritis with acute articular rheumatism is very rare. In twenty-six years' experience in the Philadelphia General Hospital, de Schweinitz has

<sup>1</sup> Section on Ophthalmology, American Medical Association, p. 262.

<sup>2</sup> Breslau Thesis, Klinische Monatsblätter für Augenheilkunde, July, 1913, p. 110.

<sup>3</sup> Monograph, printed by the author.

seen but one patient with acute rheumatic fever, who also had uveitis, and this agrees with the experience of others. Its coincidence with chronic muscular rheumatisms, "rheumatic" myalgias, may depend on a common causation. The association of uveitis with chronic polyarthritis is more frequent. He has seen at least 5 cases of this kind, although polyarthritis is an unusual disease. The dependence of uveitis upon gout is not so generally admitted as formerly. It is entirely probable, but the relation is vague. Diabetes is occasionally associated with uveitis.

Uveitis due to *gonococcus infection* may precede, accompany, or follow other manifestations of the disease. In one reported case, an intense iridoeyclitis occurred thirty years after the first and only attack of gonorrhea, the gonococci being demonstrated in the urine. In other cases, the interval has varied between four and twenty years. In such delayed cases probably some local lesion, as changes produced by eye-strain, has been the starting-point of the uveitis. While the percentages of cases ascribed to this cause is small, it is probable that thorough investigation by modern methods, including examination of centrifugalized urine, would considerably increase this percentage.

An extremely important cause of uveitis is *oral sepsis*. Lang,<sup>1</sup> among 215 cases of uveal inflammation, ascribed 139 to *pyorrhea alveolaris*. The uveitis has, however, been due to a hidden *abscess* at the root which has sometimes remained undiscovered in spite of repeated dental examinations. Uveitis proceeding from the *tonsils* or the pharyngeal arch has occasionally been observed. Infections of the nose and nasal *accessory sinuses*, which have of late attracted wide attention as a cause of ocular disease, are quite liable to set up uveitis. Eight cases of the kind are given by de Schweinitz, as reported to him by colleagues. Menstrual and uterine disorders, chronic appendicitis and boils, are also held responsible for inflammations of the uveal tract.

In most of the uveal inflammations, it is probable that the living bacteria reach the uveal tract, and by their presence and toxins, cause the inflammation. Auto-intoxication should refer only to poisons formed during metabolism within the body; and gastro-intestinal intoxication is a better term than auto-intoxication as generally applied. The study of patients from the metabolic standpoint, however, may lead to the establishment of a group of diseases of the uveal tract due to bacterial infections arising from the intestinal tract.

**Sympathetic Ophthalmitis.** McReynolds<sup>2</sup> finds that of 160 cases of sympathetic ophthalmitis, only eleven followed retention of a foreign body within the eyeball; one hundred and thirteen followed accidental injury without retention of a foreign body, and thirty-nine followed operations on the eye, most frequently cataract extraction. He finds

<sup>1</sup> *Lancet*, May 17, 1913, p. 136.

<sup>2</sup> *Trans. American Academy of Ophthalmology and Oto-Laryngology*, 1912, p. 121.

that there is no wound of the eyeball that will inevitably produce sympathetic ophthalmia, and no premonitory symptoms that can be relied on to tell when it is impending. If an eye is hopelessly lost, it should at once be enucleated; enucleation being safer than any of its substitutes. To save any seriously injured eye or utilize the benefits of any intra-ocular operation, the possibilities of sympathetic ophthalmia must be faced; and the patient must be willing to share with the surgeon the responsibility of such risk. In the discussion of McReynolds' paper, a safe attitude toward such risks was thus stated by Wescott: "I have no interest in an eye blind and useless as a result of traumatism, except to remove it at the earliest possible moment; and just as soon as I am satisfied that useful vision cannot be restored, I remove it, or withdraw from the case."

Pechdo<sup>1</sup> referring to a case in which the exciting eye still retained some vision, enucleated it, and saved better vision in the sympathizing eye. If the sympathizing eye were hopelessly lost he would favor its removal, to give the best chance to the injured eye, if it retained some vision. Cases of sympathetic ophthalmia are rare. McReynolds finds that a busy oculist will see from 5 to 10 cases in his professional life. But they are to be kept rare by keeping before the profession the gravity of the disease, and the only certain method of preventing it.

## GLAUCOMA.

**Pathogenesis.** FISCHER'S THEORY OF EDEMA, as due to increased affinity of the tissue colloids for water, was based partly on experiments that demonstrated the swelling of the eyeball when placed in slightly acid solutions; and one of the first suggestions of its practical application was to the treatment of glaucoma by use of sodium citrate solutions.<sup>2</sup> Ruben,<sup>3</sup> experimenting on pigs' eyes, measured the increase in tension of the eyeball with the tonometer and manometer. The tension increased most rapidly in the stronger solutions, and also fell sooner. In a 1 to 4 solution it reached a maximum of 134 mm. in one hour, and fell to 82 mm. in five hours. In a solution of 1 to 110 it reached the maximum of 134 mm. at five hours, and maintained it at the end of forty-eight hours. Ruben finds that the swelling occurs, not in the vitreous, as Fischer believed, but in the cornea and selera. The isolated cornea and selera placed in a solution of hydrochloric acid, 1 to 110, increased to almost ten times its original weight in twenty-four hours. Ruben believes, therefore, that the ocular tension is increased, not by swelling of the contents of the eyeball; but by reduction of its capacity, through

<sup>1</sup> L'Ophtalmologie Provinciale, vol. ix, p. 165.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1911, p. 373.

<sup>3</sup> Graef's Archiv für Ophthalmologie, vol. lxxxvi, p. 258.

swelling of the sclerocorneal coat. Removal of the eyeball into sodium citrate solution brought rapid decrease in tension, from 134 mm. to 5 mm. in 28 minutes. Return to the acid solution again increased it to 134 mm. in forty-one minutes.

By subconjunctival injections of strong solutions of hydrochloric acid,  $\frac{1}{3}$  to  $\frac{1}{10}$ , Ruben produced increase of intra-ocular tension in the living eye, reaching a maximum of 38 mm. to 100 mm. of mercury within fifteen minutes. Ruben also cites three cases of men whose eyes were injured by a caustic or a burn in whom, when seen one-half to three hours after the accident, the tension of the injured eyeball was found increased from 4 to 17 mm. Kümmell<sup>1</sup> finds a moderate rise of intra-ocular tension occurs after all burns or corrosive injuries. This begins after four or five days and generally lasts a week or two.

The idea that swelling of the sclera is capable of rapidly raising the tension of the eyeball is very suggestive. Possibly all operations that include incision of the sclera may lessen the intra-ocular tension by decreasing the scleral swelling. The general use of the tonometer is revealing increase of intra-ocular tension in various ocular conditions other than glaucoma. Injuries to the crystalline lens have long been known to cause increased intra-ocular tension. It is shown, by the above cases, that a different class of injuries may give rise to it.

Orr<sup>2</sup> states that increase of intra-ocular pressure occurs fairly frequently without causing glaucoma, and challenges the view that the essence of glaucoma lies in the increase of intra-ocular pressure. The reviewer has seen tension of 45 to 50 mm. of mercury in what appeared to be normal eyes; and 50 mm. or upward in cases of iritis. It would be more in accord with our present knowledge to say that glaucoma is characterized by a prolonged or permanent loss of balance between intra-ocular tension and the forces that sustain metabolism; so that the nutrition of the ocular tissues becomes impaired.

**The Newer Operations for Glaucoma.** These continue to receive a great deal of attention from ophthalmologists. The visit to this country of Col. R. H. Elliot, formerly of Madras, India, during which he performed his operation of sclerocorneal trephining 135 times in twenty-eight different clinics,<sup>3</sup> convinced many American surgeons of the simplicity and value of his procedure.

Elliot's operation begins with a conjunctival incision 8 or 10 mm. back from the cornea. The conjunctival flap is carefully dissected up to the corneal margin, and dissection carefully extended into the cornea, "splitting the cornea," until a crescent of clear cornea 1 mm. or more wide appears beneath the flap. A 2 mm. corneal trephine is then applied to the cornea and pushed forward with care that it shall not catch the flap, which is turned down over the cornea, and held by a moistened cotton swab. The trephine is rotated, bearing most heavily on the

<sup>1</sup> Archives of Ophthalmology, vol. xliii, p. 50.

<sup>2</sup> Ophthalmic Review, xxxiii, p. 33.

<sup>3</sup> Ibid., vol. xxxiii, p. 44.

corneal edge, so that side cuts through first, leaving the corneal flap attached to the sclera. If the iris prolapses, both iris and sclerocorneal flap are seized with fine-toothed forceps and cut off together. The toilet of the wound is made chiefly by irrigating it, and the conjunctival flap laid back in position usually without a stitch.

This operation has attracted the attention of many German operators. Meller<sup>1</sup> has reported 178 such operations, with 389 sclerectomies after the method of Lagrange.<sup>2</sup> He finds that the method of Elliot has made it easier and safer to accomplish the purpose of Lagrange, to establish free filtration from the anterior chamber into the subconjunctival space. A most recent attempt in this direction is that of D. Priestley Smith,<sup>3</sup> who makes a conjunctival flap like Elliot, extending into the cornea, then a limbal incision with the keratome, after which he cuts out a triangular piece from the corneal flap leaving a triangular instead of a round opening between the anterior chamber and the subconjunctival space.

A wider departure from established operations, but one supported by the observations of Ruben, given above, has been made by Wicher-kiewicz.<sup>4</sup> He incises the conjunctiva 10 or 12 mm. down to the sclera in the meridian of the eyeball, between the superior and external recti muscles. Drawing the conjunctiva aside, he makes three meridional and four cross-incisions into the sclera with a small Graefe knife, seeking to go down to the choroid at the centre of some of the incisions. He has done this with the idea of permitting the sclera to stretch and thus give space for its swollen contents. Its effect in reducing the scleral swelling, which Ruben deems so important, may also contribute to its efficiency. It cannot be said that these later operations have entirely displaced iridectomy; at least for the acute cases in which iridectomy gives its best results. But the good influence they have been demonstrated to exert, the ease and safety with which they are done, and readiness with which they may be repeated, especially the trephining, make it proper and imperative to advise operation in cases of glaucoma for which iridectomy offered no great assurance of relief.

The operation that has won the position of first importance is trephining. Its most serious drawback so far discovered, is the tendency of some eyes to develop, subsequently, a low-grade chronic inflammation of the uveal tract. Elliot thinks this is best prevented by making the trephine opening well forward, as far away from the uveal tract as possible. But it is still uncertain what proportion of these cases represent a chronic uveitis, arising from causes quite apart from the operation, and continuing in spite of removal of the glaucomatous complication.

<sup>1</sup> Klinische Monatsblätter für Augenheilkunde, January, 1914, p. 1.

<sup>2</sup> PROGRESSIVE MEDICINE, June, 1909, p. 299.

<sup>3</sup> Ophthalmic Review, vol. xxxii, p. 73.

<sup>4</sup> Trans. Thirty-ninth Ophthalmological Congress, Heidelberg, p. 196.

## CRYSTALLINE LENS AND VITREOUS.

**Causes of Cataract.** Although the immediate causes of cataract must all act locally, it is certain that some of them are associated with general conditions which may have the highest practical importance. The association of *tetany* and cataract has been frequently observed. It has been studied by Hesse and Phelps<sup>1</sup> with special regard to *lamellar or zonular cataract*. Among 43 cases, they found that 35 had presented unmistakable symptoms of tetany, and if they had included doubtful cases it would have been fully 90 per cent. Of this series, only 6 cases presented unmistakable evidence of rickets. They hold that the condition of the teeth usually regarded as rachitic, is more closely associated with tetany. Other forms of juvenile cataract should also be taken as a reason to search for evidences of tetany. The theory that the cataract may be caused by tetanic contraction of the ciliary muscles is rejected; and it is held that tetany and cataract both arise from a common cause, perhaps insufficiency of the parathyroids.

Van der Hoeve<sup>2</sup> has experimented on rabbits by giving them inunctions or subcutaneous injections of naphtol. He found that the production of cataract in this way was attended with destruction of the layer of rods and cones in the retina. There was also hyperemia of the choroid and iris, and vacuolation of the epithelial cells of the ciliary body. Among twenty patients seen by Van der Hoeve, who had been treated with naphtol, only one showed clouding of the crystalline lens. But all showed hyperemia of the ocular fundus which disappeared when the administration of the drug was suspended. Naphtol was administered to four pregnant rabbits. These gave birth to thirteen young, all of which showed some form of clouding of the crystalline lens; and most of them degeneration of the neuro-epithelium, and hypertrophy of pigment cells in the retina. It is suggested, there is special reason for avoiding the administration of naphtol and similar drugs to pregnant women. Schiötz<sup>3</sup> has investigated the occurrence of cataract in a district of Norway, in which calves are affected with goitre. In eight such calves he found opacity of the centre of the lens. He also finds that cataract is more frequent among women than in men.

Fuchs<sup>4</sup> has studied the opacities of the lens that follow *corneal suppuration*. He thinks it is exceptional for anterior polar cataract to be caused by adhesion between the anterior capsule and the posterior surface of the cornea. He finds generally destruction of some cells in the capsular epithelium of the lens, with proliferation of others to

<sup>1</sup> Zeitschrift für Augenheilkunde, vol. xxix, p. 238.

<sup>2</sup> Graefe's Archiv für Ophthalmologie, vol. lxxxv, p. 305.

<sup>3</sup> Norsk Magazine for Laegevidensk, vol. lxxiv, p. 1201.

<sup>4</sup> Annales d'Oculistique, vol. cl, p. 81.

fill the gap and general thinning of the layer. Cataract may develop very quickly after corneal suppuration. It was well developed in one case in five days. In a perforating ulcer with virulent hypopion he saw the anterior capsule actually ruptured. But usually the destruction of epithelial cells by toxins contained in the aqueous seems best to account for the lens opacity.

GLASS-BLOWERS' CATARACT has been the subject of an investigation by Stein,<sup>1</sup> who used homatropine and examined the lens in each glass-worker coming to him for any trouble with the eyes. Of fifty-five examined in this way, whose ages ranged from twenty-eight to sixty-five years, twenty-eight had cataract. The youngest with cataract was thirty years; the oldest free from cataract, fifty-five years. He concludes that the cataract usually begins at the posterior pole of the lens in the left eye, the left side of the face being the side toward the oven. In only one case was the right eye affected before the left; and this was in a workman who, contrary to the usual custom, had exposed the right side to the heat instead of the left.

CATARACT FOLLOWING INJURY. After an injury to the eye such as is liable to cause cataract, it is not safe to promise freedom from danger of this sequel even after several weeks. This is especially true of *electric injuries*, either by lightning-stroke or high voltage industrial currents. Culbertson<sup>2</sup> saw a woman, aged twenty-one years, seven weeks after she had received a shock that rendered her unconscious, when lightning struck the telephone she was using. At this time her eyes were severely inflamed, but vision was normal in each. Seven months later she returned with the left eye blind and the right almost blind from soft cataract. Mills<sup>3</sup> saw a man, aged twenty-eight years, rendered unconscious for seven hours by an 11,000 volt current, and kept two and one-half months in the hospital. Seven months after the accident the left eye lost sight, and a month later the right vision being reduced to counting fingers. At the end of a year the cataracts were still immature, but one was removed, giving good vision.

On the other hand, quite marked opacities of the lens, apparent shortly after a *contusion* of the eyeball, may clear up entirely. Prélat<sup>4</sup> has studied such opacities by experimenting on the eyes of rabbits, by shooting the eye with an arrow tipped with an India-rubber ball. This caused transient opacities which were found to be due to injury of the subcapsular epithelium, the capsule remaining intact. A more uncommon form of injury to terminate in spontaneous recovery is where the capsule is ruptured. Dudley<sup>5</sup> saw a man, aged sixty-six years, in

<sup>1</sup> Archiv für Augenheilkunde, vol. lxxiv, p. 53.

<sup>2</sup> American Journal of Ophthalmology, vol. xxx, p. 257.

<sup>3</sup> Archives of Ophthalmology, vol. lxii, p. 395.

<sup>4</sup> Archives d'Ophthalmologie, vol. xxxiii, p. 528.

<sup>5</sup> Ophthalmology, vol. x, p. 492.

whom the lens was broken by an explosion which caused foreign bodies to be embedded in the cornea, but without any completely penetrating wound. The injured lens was gradually absorbed, so that with the proper glass he regained vision of 20-40. Five cases of *ring-shaped clouding* of the lens near its anterior surface, that follows a contusion of the eyeball, are reported by Purtseher.<sup>1</sup> Of these, the opacity disappeared completely in the four that were followed to the end.

**SPONTANEOUS RECOVERY FROM SENILE CATARACT.** The spontaneous absorption of a senile cataract is a rare occurrence; but occasionally results in restoration of good vision. In the last year 3 cases have been reported. One seen by Verrey<sup>2</sup> was of a man who had been highly myopic. Both eyes became cataractous; one was operated on with good result; the other, left to itself, ultimately regained good vision through spontaneous resorption of the lens. Kellogg<sup>3</sup> saw 2 cases in each of which but one eye was affected, the other retaining good vision throughout. It is to be noted that in each of these cases the cataract appeared at an early age; in two of them at forty; and in the third probably earlier; and the result was only reached after many years, nineteen, twenty-four, and thirty. The occurrence of such cases keeps alive an impression among the laity that cataract can be cured by absorption. But the physician would hardly feel justified in advising a patient to wait twenty-years on the small chance for such restoration of vision without operation.

**DELIRIUM AFTER CATARACT EXTRACTION.** Postoperative delirium following the removal of senile cataract has a general significance that bears on the treatment of all elderly patients. Parker<sup>4</sup> reports 11 cases occurring among 376 patients operated on for senile cataract. The significant fact brought out by his statistics is that these patients averaged eleven years older than those who did not manifest delirium. Symptoms were noticed in from twenty-four hours to six days after the application of the bandage. In all cases, the delirium was worse at night. But, in five, it was also noticed during the daytime. None of the patients had shown signs of mental disturbance before, or at the time of operation. All but three had recovered before the usual time of leaving the hospital. None of them had been subjected to the stronger mydriatics, or to a general anesthetic, the operation being done under cocaine. None had fever.

Apparently the patients were undergoing senile changes that had so far lessened their mental stability as to allow the excitement of operation, followed by closure of both eyes and unusual quiet, to upset their mental equilibrium. That blindness with its consequent interference

<sup>1</sup> Centralblatt für Augenheilkunde, vol. xxxvii, p. 282.

<sup>2</sup> American Journal of Ophthalmology, vol. xxx, p. 300.

<sup>3</sup> Journal Ophthalmology, Otology, and Laryngology, vol. xix, p. 360.

<sup>4</sup> Section on Ophthalmology, American Medical Association, 1913, p. 395.

with normal processes may predispose to the condition, is indicated by the cases that occur while the patient is suffering from cataract and promptly recover after the cataract is removed.<sup>1</sup> The treatment of this complication is immediate freedom of the eye not operated on, with possibly small doses of some narcotic, like opium or belladonna. Prevention might sometimes be effected by avoiding, as much as possible, removal of the patient from ordinary surroundings and occupations. Lessened adaptability is a characteristic of senile change.

**LEARNING TO SEE AFTER CONGENITAL CATARACT.** *Congenital cataract* cured when the patient is old enough to respond to tests and give some account of his sensations throws light on the development of the visual function. Augstein<sup>2</sup> reports the case of a boy, aged fifteen years, suddenly relieved of a thick, capsular cataract. For three weeks he behaved as though still blind, recognizing objects entirely by touch. In the fourth and fifth weeks he began to recognize objects and persons by sight, and to avoid running against large objects that he looked directly at (central fixation). From the fifth week he learned rapidly. Common objects formerly known by touch and once seen were again recognized at different distances, and from different points of view, and he learned to avoid objects seen in the peripheral field. Nystagmic oscillations of the eye ceased after eight weeks and he was able to go on the street alone. Within five days after putting on correcting glasses, his vision rose from counting fingers to 5/50.

Moreau,<sup>3</sup> in a boy operated on for bilateral cataract at the age of eight years, also observed that on first removal of the bandage the child showed no emotion, and gave no indication of useful sight. When, however, he first acquired a new concept, as that of color, it assumed an exaggerated importance and everything was interpreted from that point of view. Moreau concludes that education of the occipital lobe must be added to the gain in ocular function before vision can become serviceable. This observation is not new. Hirschberg<sup>4</sup> points out that in Fox's *Book of Martyrs* (1563) a false miracle of restoration to sight is exposed by the impostor being able to name colors correctly. But only now are such cases being studied in a way to throw light on the physiology of vision.

**Hemorrhage into Vitreous.** Spontaneous recurring hemorrhage into the vitreous in young persons is a very obscure condition. It is generally followed by the formation of opaque connective tissue in the vitreous, ultimately causing permanent blindness. Oguchi<sup>5</sup> has made an experi-

<sup>1</sup> PROGRESSIVE MEDICINE, June, 1911, p. 376.

<sup>2</sup> Klinische Monatsblätter für Augenheilkunde, October to November, 1913, p. 521.

<sup>3</sup> Annales d'Oeulistique, vol. exlix, p. 81.

<sup>4</sup> Ophthalmic Review, vol. xxxii, p. 332.

<sup>5</sup> Graefe's Archiv für Ophthalmologie, vol. lxxxiv, p. 446.

mental study of the subject by taking blood from a vein in the ear of the rabbit, and injecting it into the vitreous humor. He finds that it is chiefly disintegrated in the vitreous, and is removed by migratory cells; and the irritation set up by these cells causes the formation of the connective-tissue masses which permanently impair vision, the so-called *retinitis proliferans*, which he finds always preceded by hemorrhages.

Bennett<sup>1</sup> has reported the case of a woman, aged twenty-three years, apparently free from tuberculosis or syphilis, whose sight was reduced by repeated hemorrhages, which recurred for seven months in spite of various lines of medical treatment, including calcium lactate, fifteen grains three times a day, until arrangements were being made for her admission to an asylum for the blind. Then, with the calcium lactate, she was given one grain of thyroid extract thrice daily. Hemorrhages ceased and vision gradually improved, until in seven months more it reached normal in one eye, and one-third in the other, and the patient was able to resume her work as a milliner's assistant. Single cases form an inadequate basis for conclusions with regard to therapy. But a single case may be suggestive, and these rare cases of blindness are so obstinate that every such suggestion must be welcome.

### RETINA, OPTIC NERVE, AND VISUAL TRACTS.

**Color of the Yellow Spot.** The region of the macula lutea, as seen with the ophthalmoscope, does not usually present any yellow spot, similar to that seen after death. But there is reason to doubt the explanation that the "yellow spot" is simply a postmortem alteration. Lottrup-Andersen<sup>2</sup> reports a case of acute ischemia of the retina, embolism of the central retinal artery, in which the yellow appearance of the macular region was strikingly noticeable. He believes this case supports the view of Tscherning that, under ordinary ophthalmoscopic illumination, the yellow color of this part of the retina is overcome, or drowned, by the red light reflected from the choroid. In this instance the yellow coloring was visible by sodium light, daylight, gas-light, and the mercury vapor lamp.

**Retinal Changes Associated with General Disease.** In opening a symposium upon this subject,<sup>3</sup> Taylor referred to the prognoses of cases with *albuminuric* and *diabetic retinitis*. Of the former, he had seen a patient die within a few hours of the discovery of the retinal lesions, and he had watched another patient for five years after they were well marked. Ormond<sup>4</sup> reports a case seen at Guy's Hospital by different members

<sup>1</sup> Ophthalmoscope, vol. xi, p. 20.

<sup>2</sup> Klinische Monatsblätter für Augenheilkunde, December, 1913, p. 740.

<sup>3</sup> Trans. Ophthalmological Society United Kingdom, vol. xxxiii, p. 1.

<sup>4</sup> Ibid., p. 90.

of the staff in which, ten years after the retinal changes and renal disease were recognized, the patient was still in fair general condition with vision of one-third in one eye. In this case, the retinal lesions were chiefly vascular and there was no evidence of a decided toxemia.

Taylor would distinguish between true *diabetes* and what might be called glycosuric cases. The latter are usually fat rather than thin, have, as a rule, no polyuria, and the amount of sugar passed is comparatively small. One of these cases was living eight years after he had first seen it at Moorfields. In discussion, Bardsley stated he had seen cases in which the cardinal signs of *retinal vascular disease* have all been present and subsequently disappeared, the retina being restored to normal appearance and function. One of these was a case of which the description agreed with that of advanced albuminuric retinitis, yet every symptom had disappeared in about three months.

Taylor thinks the prognosis should rest less on the appearance of the retinal vessels than on the associated visceral changes, especially the renal and cardiac. Among 8 cases of *thrombosis of the retinal venous branches*, he found seven had either albuminuria or hypertrophied heart. In cases in which the blood-pressure was taken, it varied from 160 to 200 mm. Taylor finds that in *syphilis*, vascular changes, especially large hemorrhages from endarteritis, occur in very malignant cases. Possibly of similar character are two cases of hemorrhagic retinitis following injections of *salvarsan* which have been recorded by Kagoshima.<sup>1</sup>

Werner<sup>2</sup> points out that while every practitioner admits the necessity of ophthalmoscopic examination in suspected intracranial tumor, a rare and generally hopeless condition, comparatively few appreciate its importance in *angiosclerosis*, a widespread disease in which early medical advice may frequently prolong life many years. Coats<sup>3</sup> points out that the changes recognized as due to obstruction of the retinal circulation, first associated with embolism, are essentially the changes of arteriosclerosis. In discussion, this view was also expressed by Straub, who believes that the culmination in obstruction may be due to conditions of atmospheric pressure, because such cases frequently occur in groups. One of his colleagues and other prominent men having died in a certain month of obstruction of the coronary artery, he saw in the next few weeks 15 cases of retinal venous thrombosis. This group of cases he followed up; and, at the end of five years, only six of these patients survived. These six included the youngest two and oldest two in the group. Between fifty and sixty-five years of age, the prognosis was particularly unfavorable. Such patients should give up arduous work and live simply, being liable to die from apoplexy, disease of the coronary artery, or nephritis.

<sup>1</sup> Nippon Gankakai Zasshi, June, 1913.

<sup>2</sup> Trans. Ophthalmological Society United Kingdom, vol. xxxiii, p. 9.

<sup>3</sup> Ibid., p. 30.

Harman<sup>1</sup> points out that some of the cases of *headache* referred to the oculist are really due to the early changes of arteriosclerosis, which may, or may not, show in the retinal vessels. He has also found that sometimes the treatment to reduce blood-pressure caused a depression that was less bearable than the pain. Gordon-Holmes insists that arteriosclerosis is often very unequally distributed. Sometimes it will be shown by a single retinal vessel. In other cases where the retinal vessels are greatly involved, the cerebral vessels may almost entirely escape, and *vice versa*. The discussion was one of great interest and general importance, worthy of a wider reading than it is likely to get in the annual volume of a special society.

**Retinitis Pigmentosa.** This is a form of retinal degeneration in which the pigment changes that give it the name are not more characteristic than the night blindness, contracted visual field, and narrowing of the retinal vessels. There has long been recognized a group of cases in which the latter symptoms were present without characteristic pigment deposits, often spoken of as *retinitis pigmentosa* without pigment. In another group *retinitis punctata albescens*, instead of pigment spots, have been found rounded whitish dots scattered through the retina. A case of this kind is described by Zani in a man, aged thirty-three years, with night blindness, contracted fields, and very slow adaptation of the retina.

As his last contribution to ophthalmic science, Nettleship<sup>2</sup> has reported such cases watched through periods of eight to twenty-seven years. A boy, who suffered from night blindness without pigmentation, afterward developed an abundance of the characteristic pigment. A man, who first noticed his night blindness after he had studied medicine, found it to progress with impaired vision, contracted fields, and narrowing of the retinal vessels. But only after twenty years was one characteristic pigment spot found in the periphery of his retina. In one case, the typical picture of *retinitis punctata albescens*, which had remained unchanged for eighteen years, gradually gave place to choroidal sclerosis and a few pigment patches typical of *retinitis pigmentosa*.

The etiology of *retinitis pigmentosa* has been obscure. Of late years studies of its pathologic histology, like that made by McKee,<sup>3</sup> have indicated that the migration of pigment cells into all parts of the retina, and their grouping about the vessels, follow sclerosis and obliteration of the more superficial choroidal vessels, particularly marked, as Nettleship long ago pointed out, in the zone where the anterior and posterior vessels anastomose. But the causes of such vascular changes are still unsettled. *Heredity, consanguinity* of the parents, and *syphilis* have

<sup>1</sup> Annali di Ottalmologia, vol. xlvi, p. 46.

<sup>2</sup> Royal London Ophthal. Hosp. Reports, vol. xix, p. 123.

<sup>3</sup> Ophthalmoscope, vol. xi, p. 408.

been most generally accepted as etiologic factors. As bearing upon the last, Usher<sup>1</sup> has collected 46 reported cases, and added 35 of his own, in which the patient was subjected to the Wassermann test. Of these, 66 gave a positive reaction, and 15 were negative. Usher points out that while a positive Wassermann proves syphilis, the negative does not exclude it. But, on the other hand, there is the chance, illustrated by 2 cases of his series, of a patient who already has retinitis pigmentosa, acquiring syphilis, and so giving a positive Wassermann.

Nettleship's studies in heredity included 976 families in which this disease was manifest, without consanguineous marriages, while in 4 per cent. more, consanguinity also entered as a factor. Usher points out that these proportions may be vitiated, on the one hand, by a tendency to report more of the instances in which heredity or consanguinity had been traced. But, on the other hand, the extreme imperfection of most family records would tend to minimize the importance of these factors. Usher's own studies include forty pedigrees. In twenty-three, the members of the family first examined gave a negative Wassermann; in four, a positive Wassermann, and in thirteen families the test was not applied.

These cases examined numbered 69, forty-two males and 27 females. Two-thirds of the patients were noticeably affected before twelve years of age. There was a greater tendency to the disease in the younger children of the family. From the first to the third child, the actual number increased; and more than half of the cases occurred among later children, indicating a factor of maternal exhaustion or parental senility. Seventeen childships furnished two or more cases each. Where the affected siblings were successive, two of the group were first born, and five were last born. Thirteen, or possibly fifteen, of the sixty-nine were mentally affected. There were eleven deaf mutes; and some deafness was noted in nineteen others. The causes to which the condition was ascribed in particular families or particular cases constitute a large and miscellaneous list.

**Detachment of the Retina.** The experience of 281 American oculists supposed to include something like 25,000 cases of detachment of the retina was collected by Vail.<sup>2</sup> Of these, 250 reported they had not seen a single permanent cure; while 31 had met with cures; 41 cases in all. But, from the records submitted, Vail was not convinced that a permanent cure was effected in more than one-half of these cases—less than one in one thousand cases treated by all the various methods that have been recommended. In view of this unfavorable prospect, Vail holds we are not justified in resorting to anything but the mildest and most humane measures "until we have a cure that cures." Hope now seems to attach itself to operative methods. In Vail's paper, Savage reports

<sup>1</sup> Royal London Ophthalmic Hospital Reports, vol. xix, p. 130.

<sup>2</sup> Trans. American Academy of Ophthalmology and Oto-Laryngology, 1913, p. 29.

striking improvement from subconjunctival injections of sodium citrate, which he thinks justifies "the hope of very frequent cures."

Fehr<sup>1</sup> has tried operation in 33 cases followed by a compressive bandage. He punctures the sclera with a broad cataract knife, and turns it to allow free escape of fluid. He reports that in 14 cases the operation failed. Five had a relapse after three months, and ten gave prospects of permanent cure at the end of periods ranging from three weeks to five years. As one case, however, relapsed after three and one-half years, it cannot be claimed that any case is permanently cured. Müller<sup>2</sup> claims five cures out of 15 cases, operated on by excising a piece of the sclera and bringing the margins of the opening together by stitches.

**Quinine and Tobacco Amblyopia.** The possibility of harm from familiar drugs is one of which the profession and laity need to be frequently reminded. Quinine and iron are associated as familiar tonics, and thought of as remedies that "can do no harm." Terrien and Aubineau<sup>3</sup> report the case of a woman, aged forty-six years, who for menstrual disturbance took capsules, which each contained about 5 grains of quinine with iron. The capsules were old, so she feared they had lost their strength and took twenty in succession. She became deaf, blind, and unconscious, with dilated pupils and filiform retinal vessels. After ten days, sight began to return in a greatly restricted field. It gradually improved under hypodermic injections of strychnine, until, in one eye, central vision rose to 8/10. But the retinal vessels remained greatly contracted, the optic disk became pale; and, after suspension of treatment, her vision was said to have declined.

NICOTINE, a drug even more powerful than quinine, is also in more familiar use. So many users of tobacco escape toxic amblyopia that the question is sometimes raised whether tobacco alone can cause it. To the recorded cases, which clearly answer this question in the affirmative, one is added by Foster.<sup>4</sup> A man, aged sixty-five years, an inveterate smoker, came with vision reduced to 20/200. But, after stopping the use of tobacco, it rose in two weeks to 20/50, and with strychnine taken internally and subcutaneously for eleven months vision of 20/15 was recovered. The patient was free from any signs of syphilis, tuberculosis, etc., and a total abstainer from alcoholic drinks.

**Anomaly of Optic Nerve.** A case of division of the optic nerve into two trunks, a little in front of the chiasm, is reported by Sneed.<sup>5</sup> A man, aged sixty-six years, died of cirrhosis of the liver without ophthalmoscopic examination, and with no ocular symptoms. At the autopsy, the right optic nerve was found to divide into a large trunk 4 mm., and

<sup>1</sup> Graefe's Archiv für Ophthalmologie, vol. lxxxv, p. 336.

<sup>2</sup> Klinische Monatsblätter für Augenheilkunde, August, 1913, p. 254.

<sup>3</sup> Archives d'Ophtalmologie, vol. xxxiii, p. 699.

<sup>4</sup> Trans. American Ophthalmological Society, vol. xiii, p. 516.

<sup>5</sup> Archiv für Augenheilkunde, vol. lxxvi, p. 117.

a smaller one  $2\frac{1}{2}$  mm. in diameter. These reunited before reaching the eyeball, and presented no pathological changes.

**Retrobulbar Neuritis.** It is suggested by Cross<sup>1</sup> that cases of retro-ocular neuritis may be due to hemorrhage hidden in the axis of the nerve. He mentions a case of the kind in which, a week or two after the appearance of the central scotoma, a small hemorrhage appeared in the optic disk. The case subsequently ran the course of a retro-ocular neuritis to a complete recovery. The analogy between such cases and those of thrombosis of a retinal vein is not difficult to trace.

**Optic Neuritis from General Causes.** A case of optic neuritis arising as a sequel to *measles* is reported by Santos Fernandez.<sup>2</sup> Loss of sight was noticed soon after the disappearance of the eruption, and the pupil became dilated. There was some swelling of the optic disk. With injections of antidiphtheritic serum, improvement in vision began the day after the first injection; vision became normal in four weeks, and continued so five months later.

Optic neuritis and consecutive atrophy following *pregnancy* is reported by Butler.<sup>3</sup> Two weeks after delivery of a still-born child at full term, a woman, aged twenty-four years, suffered from violent headache and vomiting, and, when seen five weeks later, presented well-marked optic neuritis. She was free from kidney disease and arteriosclerosis, gave a negative Wassermann reaction, and no reaction to old tuberculin. Vision was reduced to 3/60 in the right eye, with great contraction of the field; and 6/9 in the left with nearly normal field; and the disks became white and atrophic. Similar cases occurring after delivery have been ascribed to lactation, which had to be excluded in this case. Butler has no doubt it was caused by a *toxemia* arising from pregnancy.

**Optic Neuritis of Nasal Origin.** Paunz<sup>4</sup> divides these cases into two classes: In one, there is a distinct nasal or sinus infection; and, upon the proper treatment of this infection, the optic nerve recovers. In the second class, no marked disease of the nose or nasal sinuses is discovered. But, upon drainage or treatment of the sinuses, the optic neuritis rapidly subsides. He thinks the connection of these latter cases with the nose is not imaginary. He reports two of each class. One case, originally of the first class, suffered a relapse during which little disease was discoverable in the nose, yet under treatment the optic nerve condition recovered as it had done a year before when treated for a notable ethmoidal suppuration.

Cases of optic neuritis occurring with disease of the sphenoid or ethmoid have frequently been reported. But the case of optic neuritis arising directly from *suppuration of the maxillary antrum* reported

<sup>1</sup> Trans. Ophthalmological Society United Kingdom, vol. xxxiii, p. 43.

<sup>2</sup> Archivos de Oftalmología, Hispano-Americanos, vol. xiii, p. 350.

<sup>3</sup> Ophthalmoscope, vol. xi, p. 597.

<sup>4</sup> Archiv für Augenheilkunde, vol. lxxv, p. 76.

by Foster,<sup>1</sup> seems to be the first of the kind recorded. A young man, who had suffered from influenza and very severe pain in the left side of the head and face for two weeks, came with vision reduced to 6/60, some swelling and tenderness in the lower part of the orbit, and ophthalmoscopic evidence of optic neuritis. Drainage and washing out of the antrum were followed by recovery within one week. In this case, Foster was unable to find any evidence of a defect in the floor of the orbit.

Pooley and Wilkinson<sup>2</sup> have recorded a case in which a cyst of the maxillary antrum caused bulging of the bony wall into the orbit, and, apparently by pressing the optic nerve against the upper edge of the foramen, obliterated vision by "a dark line" slowly rising from the lower part of the field, and rendered the pupil insensitive to light. Tapping of the cyst was followed by immediate return of vision, which, in twelve days, had improved to 6/9, and within a month to 6/5. In this case the antrum appeared to be an entirely closed cavity, with unusually thick outer and nasal walls, and a closed ostium.

**Permanent Hemianopsia after Migrain.** Temporary blurring of sight in one-half the field of vision is a common prodromal symptom of migrain. Ormond<sup>3</sup> has collected other reported cases, and added two of his own in which severe migrainous attacks have been followed by permanent hemianopsia, without much other evidence of a cerebral lesion. He thinks the probable explanation is that migrain depends on arterial spasm followed by a dilatation; and that, in these cases, the spasm was sufficiently severe and prolonged to permit thrombosis of the branch supplying the visual cortex in one occipital lobe. In discussion, Holmes, who had seen a similar case in which there was some arteriosclerosis, pointed out that it was difficult to exclude vascular changes.

**Blindness from Brain Abscess.** Two cases in which acute blindness was the first positive symptom of brain abscess are reported by Pagenstecher.<sup>4</sup> One patient was a clerk, aged twenty-five years, previously in good health, who, for eight days, had suffered severe headache and twice had vomited. During this time, vision rapidly declined until only perception of hand movements remained. The eyes, including the fundus as seen with the ophthalmoscope, appeared normal. Two days afterward the patient felt better and regained some vision, but after four convulsive seizures he suddenly died. He was found to be suffering from gangrenous bronchopneumonia; and had a large metastatic abscess in the right occipital lobe, with a smaller one in the left parietal lobe. A stone-cutter, aged thirty-seven years, suffered from

<sup>1</sup> Ophthalmic Review, vol. xxxii, p. 329.

<sup>2</sup> Ibid., vol. xxxii, p. 130.

<sup>3</sup> Trans. Ophthalmological Society United Kingdom, vol. xxxiii, p. 138.

<sup>4</sup> Archiv für Augenheilkunde, vol. Lxxv, p. 2355.

pulmonary disease for six years. He had headache for two weeks, when he noticed disturbance of sight and the next day could not find his way about. Ophthalmoscopically and otherwise both eyes appeared normal, except that the pupils were dilated and reacted very sluggishly to light. The eye-grounds continued normal until death, three days later. Autopsy showed pulmonary tuberculosis, with gangrene in the left lower lobe, and metastatic abscess in each occipital lobe of the brain.

### LIDS, LACRIMAL APPARATUS, AND ORBIT.

In a case of traumatic facial paralysis, resulting from an automobile accident, Dutoit<sup>1</sup> observed a symptom that he does not find mentioned in the literature. The patient was able to close the lids by rotating the eye outward. At first it required a strong outward movement to do this; but gradually less turning of the eye was necessary, and, after three months, he could close the lid by merely thinking of the outward rotation. At first attempts to raise the lid merely caused the affected eye to roll upward. Dutoit supposed strong effort to close the eye caused inhibition of the other ocular muscles, so it turned up as it would in sleep. An involuntary impulse to laugh caused closure of the eyes. After repeated attempts to close them, there was an involuntary elevation of the angle of the mouth on the affected side.

**Gangrene of the Lids.** Bossalino<sup>2</sup> reports a case of this rare condition occurring in a man, aged twenty years, who, four days before, had received a slight injury to the lid. The following night the patient had a chill and the lid was swollen. When seen, there was intense edema of the lids and neighboring parts; and a large black eschar reaching from the brow almost to the ciliary margin of the upper lid. Pyrexia continued about three days longer, the temperature running to 40° C. A very similar case is reported by Leplat, Rivière, and Bettremieux<sup>3</sup> in a man, aged twenty-four years, who thought he had been bitten on the lid by an insect four days before. When seen, his temperature was 40.2° C., and fever did not subside until four days later. There was at first a vesicle and, later, a large black eschar. On the clinical appearances, and perhaps the fact that the patient worked in a woollen mill, a diagnosis of *anthrax* of the lids was believed justified. Bossalino supposed his case was due to a *streptococcus* infection. In both cases, the bacteriological examination proved negative, except that Bossalino found the white staphylococcus. It is probable that all cases of lid gangrene are due to some malignant infection; although up to the present time the results of bacteriological examinations have generally been negative.

<sup>1</sup> Graefe's Archiv für Ophthalmologie, vol. lxxxvi, p. 145.

<sup>2</sup> Annali di Ottalmologia, vol. xli, p. 610.

<sup>3</sup> La Clinique Ophthalmologique, vol. xix, p. 621.

**Tuberculosis of the Lacrimal Sac.** The harmful influence of mechanical obstruction of the tear passages is so obvious, and measures for its removal have claimed so much attention, that all sorts of cases of lacrimal disease have been subjected to the same mechanical treatment without much thought as to possible causation. The mechanical method of removing the diseased tissue by extirpation of the sac has furnished material for microscopic study, and this in turn has directed attention to the etiology. *Syphilis*, especially where it involved the bones, has long been recognized as an important cause. Tuberculosis seems likely to prove of equal importance. Butler<sup>1</sup> adds to these, as important causes in the child, failure of the passage to become patent, and, in older patients, trachoma.

Often the diagnosis of tuberculosis has had to rest upon histological changes without the recognition of the bacillus, except by inoculation experiments. In a case reported by Wittich,<sup>2</sup> of a girl, aged eighteen years, who had shown enlarged cervical glands for two years, and swelling of the lacrimal sac for six months, both histological structure and tubercle bacilli gave evidence of the cause. In this case, numerous typical tubercles were present, especially around the canaliculi, where the process seemed to be extending. On this account, Wittich advises removal of as much of the canaliculi as possible with the sac.

General treatment is of value in these cases, but no one cares to rely on it to the exclusion of thorough extirpation of the local lesion. Rollet and Genet<sup>3</sup> report of a girl, aged sixteen years, coming of a tuberculous family, whose symptoms were those of acute dacryocystitis. But, when the lacrimal sac was extirpated, inoculation of the guinea-pig proved tuberculosis. After eleven months swelling had recurred, and a new mass of tuberculous tissue was removed. Two years later a tumor appeared in the lacrimal region of the other side, which was found to be located in front of the sac.

Fage<sup>4</sup> suggests that after extirpation of a sac that is found to be tuberculous, recurrences, or persistent fistulæ, are to be dealt with by the application of the galvanocautery. He reports a case, in which tuberculosis also involved the apices of both lungs. He divides the cases of lacrimal tuberculosis into those in which the tumor is prelacrimal, those localized in the sac, and lesions involving the bones adjoining the sac.

**Traumatic Pulsating Exophthalmos.** Pulsating exophthalmos following severe injury to the head, usually with decided bruit, and presumably caused by arteriovenous aneurysm due to rupture of the carotid artery into the cavernous sinus, has often been treated by lig-

<sup>1</sup> British Medical Journal, November 1, 1913, p. 144.

<sup>2</sup> Klinische Monatsblätter für Augenheilkunde, May, 1913, p. 577.

<sup>3</sup> La Clinique Ophtalmologique, vol. xix, p. 734.

<sup>4</sup> L'Ophtalmologie Provinciale, vol. ix, p. 114.

tion of the common carotid artery. To the average surgical mind this appeals as a most rational procedure; and it is justified by the extremely annoying character of the bruit sometimes present, and the deformity persisting in spite of medical treatment and compression of the carotid. But this serious operation, which has sometimes caused blindness and sometimes death, through its effect on the cerebral circulation, should be avoided until the less serious operation of *tying the enlarged orbital veins* has been tried, especially as the latter has proved more likely to give relief.

Three cases from the literature of the past year enforce this lesson. Feruglio<sup>1</sup> saw a boy who received a penetrating wound on the lower lid followed by vomiting, headache, mental disturbance, and exophthalmos. There was marked pulsation of the retinal veins synchronous with the arterial pulse. The common carotid artery of the affected side was tied without favorable result. Ginsburg<sup>2</sup> saw a boy, aged eighteen years, rendered unconscious by a blow on the head, who showed evidence of fracture through the sella turcica, with rupture of the optic nerve, and of the internal carotid in the cavernous sinus. Ligation of the common carotid on the affected side was of little benefit. So three months later the angular, frontal, supra-orbital, and superior palpebral veins were tied and divided, giving complete and permanent relief. Buchtel<sup>3</sup> saw a boy, aged eleven years, struck on the head by a pitch-fork three months before. He presented exophthalmos and a bruit from a few days after the injury. After comparing the recorded experiences regarding the two operative measures, he tied the angular, superficial temporal, superior ophthalmic, and numerous superficial veins. The bruit ceased at once, and the exophthalmos rapidly subsided.

**Removal of Conjunctiva and Lid Margins with the Eyeball.** For patients who, for any reason, cannot wear an artificial eye, the usual empty orbit is a continual source of discomfort and annoyance. Complete removal of the conjunctiva with the lashes and lid margins, permitting the union of the lids with each other, and the deeper tissues, give a smooth skin surface that is far less unsightly than the ordinary empty socket, and requires not the slightest attention on the part of the patient. Such an operation may be demanded by destruction of the lids, malignant disease requiring their partial removal, contraction of the socket so that a sightly artificial eye cannot be worn; or even on account of the poverty of the patient, who may be unable to purchase an artificial eye.

Such an operation was reported years ago by the later Dr. John Green, but has not received the general attention it deserves. MacNab<sup>4</sup> describes the technique that he has devised to meet the needs of patients

<sup>1</sup> Annali di Ottalmologia, vol. xlvi, p. 286.

<sup>2</sup> Klinische Monatsblätter für Augenheilkunde, December, 1912, p. 698.

<sup>3</sup> Ophthalmic Record, vol. xxii, p. 75.

<sup>4</sup> Trans. Ophthalmological Society, United Kingdom, vol. xxxviii, p. 50.

who have required enucleation, but who have been unable to have an artificial eye. Each lid is incised down to the tarsal plate, except toward the nasal end. The two incisions are joined by a cut with scissors that divides the external ligament. The lid margins and attached conjunctiva are then drawn toward the nose, and separated from the orbital tissue by blunt pointed scissors. If the conjunctiva is thin and loose, it is better to introduce the forefinger into the sac to stretch it, while being separated from the deeper tissues. The mass thus gathered together is finally separated by a cut at the inner canthus. The skin margins are then brought together by four sutures. When remains of a shrunken globe are present, this should be brought away with the conjunctival tissues. When the full-sized globe is to be dealt with, first the lower, and then the upper portion of the conjunctiva is to be dissected up; and afterward the eyeball separated from the deeper attachments.

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